

REGULATING HEALTH AND WEALTH

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The SEC and FDA are two of the nation's most prominent agencies, and both are charged with protecting the public. The agencies are children of tragedy and share similar creation stories. These kindred agencies are both burdened with daunting missions and myriad challenges in executing them. Both balance protecting an unsophisticated vulgus from uncertain risk against over-regulation of sophisticated intermediaries. Yet, they have charted very different paths in trying to accomplish their missions. From the beginning, the SEC eschewed merit-regulation in favor of disclosure. In contrast, the FDA, in its quest to protect us from unsafe and ineffective drugs, grew to become the most prominent merit-regulator. Along its journey, the FDA's reputation has been sullied by approving unsafe and ineffective drugs and ultimately not fulfilling its mission. Worse yet, the FDA regulations have unduly delayed access to beneficial drugs. This Article presents the case for an end to merit-regulation in the context of prescription drugs and proffers a proposal for the FDA to adopt a regulatory model more akin to the SEC. It briefly describes the history of the SEC and the FDA and the context in which their distinct regulatory paths were forged. Then, this Article presents an overview of the drug approval process and describes its numerous shortcomings. Next, using the SEC as a model, this Article presents a proposal for the FDA to shift its regulatory focus from merit-based regulation to disclosure-based regulation. The proposal seeks to reframe the FDA's focus to the areas in which it can be most effective while increasing the public's access to drugs.

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INTRODUCTION

The drug and financial industries are twin titans in the American economy¹ and permanently embedded in American culture.² The Food

¹ See, e.g., Robert I. Field, *How the Government Created and Sustains the Private Pharmaceutical Industry*, 6 ST. LOUIS U. J. HEALTH L. & POL'Y 11, 14 (2012) ("Over the past 20 years, no American industry has outperformed pharmaceutical manufacturing in terms of profitability."); Herman Saftlas, *Healthcare: Pharmaceuticals*, STANDARD & POOR'S INDUSTRY SURVS., June 2, 2011, at 1 (noting that the pharmaceutical industry had over \$900 billion in earnings in 2010); see also Kathleen Madigan, *Like the Phoenix, U.S. Finance Profits Soar*, WALL ST. J. REAL TIME ECON. (Mar. 25, 2011, 4:53 PM), <http://blogs.wsj.com/economics/2011/03/25/like-the-phoenix-u-s-finance-profits-soar> ("After rising like the Phoenix, the financial industry now accounts for about 30% of all operating profits. That's an amazing share given that the sector accounts for less than 10% of the value added in the economy.").

² Both the pharmaceutical and financial industries have caught the fancy of Hollywood. In *The Constant Gardner* (based on a novel), the lead character Quayle's investigation of his wife's murder uncovers the practices of a fictional pharmaceutical company that tests its drugs on poor Kenyans in exchange for free health care. See Book Description of *The Constant Gardner: A Novel*, AMAZON, <http://www.amazon.com/Constant-Gardener-Novel-John-Carre/dp/B006QS5H90> (last visited Sept. 7, 2013); Editorial Reviews of *The Constant Gardner: Widescreen Edition*, AMAZON, <http://www.amazon.com/The-Constant-Gardener-Widescreen-Edition/dp/B000C65Z1G> (last visited Sept. 7, 2013). The pharmaceutical industry has also been featured in blockbusters such as RISE OF THE PLANET OF THE APES (Twentieth Century Fox 2011), LOVE & OTHER DRUGS (Fox 2000 Pictures 2010), and THE FUGITIVE (Warner Brothers 1993). The financial industry has been featured prominently in Oliver Stone's WALL STREET (Twentieth Century Fox 1987), BOILER ROOM (New Line Cinema 2000), TRADING PLACES

and Drug Administration (FDA), the agency responsible for regulating the pharmaceutical industry, monitors more than \$1 trillion worth of products, representing about a quarter of every dollar spent by American consumers each year.³ Similarly, the Securities and Exchange Commission (SEC) monitors over \$17 trillion worth of assets.⁴

Thus, the importance of both agencies cannot be understated. Yet, the industries regulated by each, namely “big pharma” and Wall Street, have recently been the subject of public opprobrium and chided for promoting corporate cultures that reward avarice and unscrupulous conduct.⁵ As scandals rocked both industries, public confidence in the bodies that regulate the industries tumbled, leaving the industries and agencies alike engulfed in a sea of criticism.⁶

(Cinema Group Ventures 1983), *THE PURSUIT OF HAPPYNESS* (Columbia Pictures 2006), and *TOWER HEIST* (Universal Pictures 2011).

³ Martin S. Lipsky & Lisa K. Sharp, *From Idea to Market: The Drug Approval Process*, 14 J. AM. BOARD FAM. PRAC. 362, 362 (2001), available at <http://www.jabfm.org/content/14/5/362.long>.

⁴ Market capitalization, the market value of all domestic listed companies, was \$17,139,000,000 at the end of the year 2010. U.S. CENSUS BUREAU, STATISTICAL ABSTRACT OF THE UNITED STATES: 2012 870 tbl.1397 (131st ed. 2011), available at <http://www.census.gov/prod/2011pubs/12statab/intlstat.pdf> (using a detailed table to examine United States and foreign stock trades between 2000 and 2010 in order to ascertain market capitalization).

⁵ The financial sector has been plagued by a series of black eyes over the last decade. The decade began with the collapse of Enron and WorldCom. See, e.g., Patrick McGeehan, *Goldman Chief Urges Reforms in Corporations*, N.Y. TIMES, June 6, 2002, at A1 (“I cannot think of a time when business over all has been held in less repute. . . . The business community has been given a black eye by the activities and behavior of some C.E.O.’s and other notable insiders who sold large numbers of shares just before dramatic declines in their companies’ share prices” (quoting Henry M. Paulson, Jr.) (internal quotation marks omitted)); Brian Faler, *TARP a “Four-Letter Word” for Voters Even as Cost Drops*, BLOOMBERG (Oct. 8, 2010, 12:00 AM), <http://www.bloomberg.com/news/2010-10-08/tarp-a-four-letter-word-for-voters-even-as-bailout-cost-estimates-plunge.html> (describing pervasive public resentment against the bailout for the large banks). Similarly, the pharmaceutical industry has been a mainstay source of news for running misleading ads, improperly influencing doctors’ prescribing patterns, and failing to notify the government of safety issues concerning their drugs. See, e.g., Natasha Singer, *A Pill That Promised Too Much*, N.Y. TIMES, Feb. 10, 2009, at B1 (reporting that as part of its \$20 million ad campaign Bayer, the manufacturer of Yaz, ran misleading ads during popular TV shows); see also *infra* Part IV.A.

⁶ See Barbara J. Evans, *Seven Pillars of a New Evidentiary Paradigm: The Food, Drug, and Cosmetic Act Enters the Genomic Era*, 85 NOTRE DAME L. REV. 419, 431 (2010) (“Public confidence in FDA fell from 80% in the 1970s to 61% in 2000; 56% in 2004; and 36% in 2006.”). A 2008 study found that 58% of participants had negative views toward the FDA’s performance in ensuring the safety and efficacy of new prescription drugs. *Confidence in FDA Hits New Low, According to WJS.com/Harris Interactive Study*, HARRIS INTERACTIVE (Apr. 22, 2008), <http://www.harrisinteractive.com/Default.aspx?tabid=446&ctl=ReadCustom%20Default&mid=1506&ArticleId=339>. For a description of public outcry in the financial context, see Tamar Frankel, *Regulation and Investors’ Trust in the Securities Markets*, 68 BROOK. L. REV. 439, 443–44 (2002) (“[W]hen the market crashes and investors lose significant amounts of money, they . . . cannot avoid a suspicion that something wrong in the system caused the crash. Losing investors suspect that the system allowed someone to gain at their expense. They begin to question the integrity of the system, and their trust falters.”).

Criticisms of the SEC and the FDA are numerous and far-reaching. The left charges that the agencies are lax in enforcement and not doing enough to protect the masses, while the right charges that regulations stifle growth and innovation. Among the most repeated criticisms is the charge that both agencies are “captured.”⁷ Worse yet, critics charge that both agencies have created burdensome and ineffective regulatory schemes⁸ that ultimately leave the public unprotected and paying higher prices for products and services.

While the critical voices often do not agree about how to fix or improve regulation of the financial and pharmaceutical industries, most critics agree that fundamental to the mission of both agencies is the notion of providing some layer of protection for the public.⁹ Although

⁷ Agency capture often occurs when the industry that the agency seeks to regulate has some control over the agency’s budget. For example, financial firms successfully lobbied Congress to cut the SEC’s budget limiting the agency’s ability to enforce existing securities regulations and discouraging the proposal of new regulation. See Elizabeth F. Brown, *E Pluribus Unum—Out of Many, One: Why the United States Needs a Single Financial Services Industry*, 14 U. MIAMI BUS. L. REV. 1, 52 (2005) (“[D]uring the 1990s, the SEC’s lack of control over its budget allowed it to be effectively captured by the securities industry that it was supposed to regulate.”). With respect to the FDA, user fees paid by drug sponsors comprise a large chunk of its budget. See, e.g., W. John Thomas, *The Vioxx Story: Would it Have Ended Differently in the European Union?*, 32 AM. J.L. & MED. 365, 372 (2006) (“[H]aving the [FDA] depend financially on the regulated [pharmaceutical manufacturers] has laid the groundwork for concerns of a system compromised by conflict of interest.”); Jamie L. Aldes, Note, *The FDA Clinical Trial Process: Effectuating Change in the Regulatory Framework Governing Clinical Trials to Account for the Historical Shift from “Traditional” to “New” Phase I Trials*, 18 HEALTH MATRIX 463, 463, 463 n.1 (2008) (“The culture within the FDA, [is] one where the pharmaceutical industry, which the FDA is supposed to regulate, is seen by the FDA as its client instead.” (quoting *FDA Failed Public on Vioxx, Scientist Says*, NBC NEWS (Nov. 19, 2004), <http://www.nbcnews.com/id/6520630/#.UbWv-5W3VUQ> (quoting Sen. Jeff Bingaman (D-NM))) (internal quotation marks omitted)).

⁸ The literature is replete with criticisms of the current SEC regulatory model and proposals for reform. See, e.g., Stephen Choi, *Regulating Investors Not Issuers: A Market-Based Proposal*, 88 CALIF. L. REV. 279, 282 (2000) (“[T]he current regime is at best inconsistent and often flawed because of its lack of focus on the impact of regulation on the choices available to investors.”); Lee Harris, *The Politics of Shareholder Voting*, 86 N.Y.U. L. REV. 1761 (2011) (arguing that SEC reforms aimed at increasing shareholder participation are not based on empirical evidence and that challengers in board elections need capital in addition to access to be successful); Usha Rodrigues & Mike Stegemoller, *Placebo Ethics: A Study in Securities Disclosure Arbitrage*, 96 VA. L. REV. 1 (2010) (finding that section 406 of Sarbanes-Oxley is ineffective and proposing that companies disclose related-party transactions involving high level managers, regardless of the company’s ethics rules). There is also a robust literature that is critical of the FDA. See, e.g., Michael J. Malinowski & Grant G. Gautreaux, *Drug Development—Stuck in a State of Puberty?: Regulatory Reform of Human Clinical Research to Raise Responsiveness to the Reality of Human Variability*, 56 ST. LOUIS U. L.J. 363 (2012) (arguing that the FDA should shift course from its historically paternalistic approach of restricting drug manufacturers’ speech to policies designed to enable the broader dissemination of truthful prescription drug information); Efthimios Parasidis, *Patients over Politics: Addressing Legislative Failure in the Regulation of Medical Products*, 2011 WIS. L. REV. 929 (2011) (criticizing the current post-marketing surveillance regulations and proposing that manufacturers conduct extensive post-approval testing in exchange for limited liability).

⁹ For a discussion of the SEC’s role in protecting the common investor, see generally Ronald J. Colombo, *Trust and the Reform of Securities Regulation*, 35 DEL. J. CORP. L. 829, 869,

their industries are different, their missions are the same. Namely, the SEC is charged with protecting the common investor,¹⁰ and the FDA is charged with protecting the health of consumers taking prescription drugs.¹¹

For the FDA, protecting the consumer takes many forms, but this Article focuses on the approval of prescription drugs. At first blush, the analogy between financial products and drugs might seem too attenuated to be useful. However, the analogy is quite useful for a few reasons. First, drugs, like financial products, are ubiquitous. Approximately 240 million Americans imbibe, ingest, inject, inhale, and infuse prescribed medications each week.¹² Americans are among the

870 n.260 (2010) (“Congress acted with ‘the specific purpose of protecting the common layperson investor, unfamiliar with the complexities of the financial markets’” (quoting Evan M. Gilbert, *Unnecessary Reform: The Fallacies with and Alternatives to SEC Regulation of Hedge Funds*, 2 J. BUS. ENTREPRENEURSHIP & L. 319, 322–23 (2009))); Jeff Schwartz, *Fairness, Utility, and Market Risk*, 89 OR. L. REV. 175, 176 (2010) (“The goal of the regulatory regime is investor protection and the primary mode of regulation is mandated disclosure.”); Ralph K. Winter, *On “Protecting the Ordinary Investor,”* 63 WASH. L. REV. 881, 882 (1988) (“Most thus agree that the goal is the protection of the investor in common shares of publicly-traded corporations.”). *But see* Zohar Goshen & Gideon Parchomovsky, *The Essential Role of Securities Regulation*, 55 DUKE L.J. 711, 713 (2006) (“Securities regulation is not a consumer protection law. Rather, scholarly analysis of securities regulation must proceed on the assumption that the ultimate goal of securities regulation is to attain efficient financial markets and thereby improve the allocation of resources in the economy.”). For a discussion of the FDA’s role in protecting the public from unsafe drugs, see generally Peter Barton Hutt, *Philosophy of Regulation Under the Federal Food, Drug and Cosmetic Act*, 28 FOOD DRUG COSMETIC L.J. 177, 181 (1973) (“Although the sole purpose of the Food and Drug Administration is to serve the public interest, there is, of course, no unitary ‘public’ that makes its views and interests known to us.”); Charles Steenburg, *The Food and Drug Administration’s Use of Postmarketing (Phase IV) Study Requirements: Exception to the Rule?*, 61 FOOD & DRUG L.J. 295, 295 (2006) (“The Food and Drug Administration (FDA) sometimes pushed the envelope of its statutory authority in the name of protecting public health.”).

¹⁰ The legislative history of the 1933 Act clearly establishes that investor protection through disclosure was the central goal. *See* S. REP. NO. 73-47, at 1 (1933), *reprinted in* 2 LEGISLATIVE HISTORY OF THE SECURITIES ACT OF 1933 AND SECURITIES EXCHANGE ACT OF 1934 (J. S. Ellenberger & Ellen P. Mahar eds., 2001) (“The aim is to prevent further exploitation of the public by the sale of unsound, fraudulent, and worthless securities through misrepresentation; to place adequate and true information before the investor; . . . to restore the confidence of the prospective investor . . .”).

¹¹ *See* STAFF OF H. SUBCOMM. ON SCI., RESEARCH & TECH. OF THE H. COMM. ON SCI. & TECH., 96TH CONG., REP. ON THE FOOD AND DRUG ADMINISTRATION’S PROCESS FOR APPROVING NEW DRUGS 1 (Comm. Print 1980) [hereinafter DRUG APPROVAL REPORT] (“The Food and Drug Administration (FDA) is a scientific regulatory agency dedicated to achieve a single, overall objective: consumer protection.”); Aldes, *supra* note 7, at 466 (“The overarching purpose of FDCA is ‘to protect the consuming public from regulated products that are unsafe . . . [or] ineffective.’ (alteration in original) (quoting A PRACTICAL GUIDE TO FOOD AND DRUG LAW AND REGULATION 47 (Kenneth R. Piña & Wayne L. Pines eds., 2d ed. 2002))).

¹² *See* Donald W. Light, *Bearing the Risks of Prescription Drugs*, in THE RISKS OF PRESCRIPTION DRUGS 1, 24 (Donald W. Light ed., 2010).

most medicated peoples in the world,¹³ with sales of prescription drugs now exceeding \$320 billion a year.¹⁴

For better or worse, the power of the pill seems to be permanently embedded in the American psyche. And it is no wonder. Americans are constantly inundated with messages about the power of a prescription. The ads are everywhere. They are in our home running during primetime television's most popular shows.¹⁵ Drug ads are in between our favorite songs that we listen to on the radio,¹⁶ at the bus stop,¹⁷ and even on Facebook.¹⁸ As a category of products, spending on the

¹³ See Steven Reinberg, *U.S. Kids Take More Psychotropic Drugs than Europeans*, ABC NEWS (Sept. 24, 2008), <http://abcnews.go.com/Health/Healthday/story?id=5880138&page=1> ("American children are three times more likely to be prescribed psychotropic medications for conditions such as ADHD and bipolar disease than European children are, a new study finds."); *Study Shows More Americans Taking Prescription Drugs*, USA TODAY (May 14, 2008, 9:19 AM), http://www.usatoday.com/news/health/2008-05-14-medication-nation_N.htm ("Americans buy much more medicine per person than any other country.").

¹⁴ IMS INST. FOR HEALTHCARE INFORMATICS, *THE USE OF MEDICINES IN THE UNITED STATES: REVIEW OF 2011 2* (2012), available at http://www.imshealth.com/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/IHII_Medicines_in_U.S_Report_2011.pdf.

¹⁵ Approximately 31.5% of advertising dollars spent by pharmaceutical companies went towards spots during primetime television. See Beth Synder Bulik, *Ad Spending: 15 Years of DTC*, AD AGE INSIGHTS WHITE PAPER, Oct. 17, 2011, at 9, available at http://gaia.adage.com/images/bin/pdf/WPpharmmarketing_revise.pdf (detailing the mediums in which pharmaceutical advertising dollars were spent).

¹⁶ See, e.g., Warning Letter from Thomas W. Abrams, Dir., Div. of Drug Mktg., Adver., & Comm'ns, Food & Drug Admin., to Michael D. Becker, President & Chief Exec. Officer, Cytogen Corp. (July 18, 2005), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm054806.pdf> (noting that the radio ad for Quadramet did not disclose risk information specific to the drug and requesting immediate cessation of the violative ads).

¹⁷ See Sabin Russell, *S.F. Ban on AIDS Drug Ads Proposed/Dubious Message in Bus Shelters*, SFGATE (Mar. 15, 2001, 4:00 AM), <http://www.sfgate.com/health/article/S-F-Ban-on-AIDS-Drug-Ads-Proposed-Dubious-2942068.php> (reporting that public hearings would be held to consider a ban on AIDS drug advertisements in city bus shelters because they portrayed too positive a picture of life with AIDS and were suspected of causing individuals to underestimate the risk of HIV infection).

¹⁸ For example, in 2010, Novartis created a website for Tassigna, its leukemia drug, that contained a "Facebook Share" media widget. The widget created information about Tassigna that could be shared with other Facebook members. The widget created content that was misleading, failed to provide any risk information, implied superiority over other products, and constituted misbranding under 21 U.S.C. § 352(a), (n) (2012) and their implementing regulations. Through an untitled letter sent to Novartis, the FDA requested that Novartis discontinue dissemination of the violative promotional materials. Letter from Karen R. Rulli, Acting Grp. Leader, Div. of Drug Mktg., Adver. & Comm'ns, Food & Drug Admin., to Dr. Lisa Drucker, Dir., Regulatory Affairs—Oncology, Novartis Pharm. Corp. (July 29, 2010), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM221325.pdf>.

marketing of pharmaceuticals is surpassed only by the automobile and fast food industries.¹⁹

Similarly, investing is a large part of American culture and integral to responsible retirement planning. Over 50% of households report investing in an employer sponsored retirement plan.²⁰ In 2012, American families held \$17.9 trillion in retirement assets.²¹ Americans rely on their prescriptions to keep them healthy and in retirement, Americans may in turn rely on investment income in order to be able to afford their many prescriptions.²² Thus, drugs and financial products are fixtures in the American existence and without proper oversight the regulatory failures are far-reaching.

Yet, the challenges of regulating such ubiquitous industries are further complicated by the fact that the masses are unsophisticated.²³ The average patient has little knowledge of basic pharmacology and must trust in the expertise of physicians.²⁴ Similarly, investors lack a basic understanding of investments. A study commissioned by the SEC found that many investors did not understand the difference between stocks and bonds.²⁵ Additionally, the agencies' proper roles in

¹⁹ Toni Fitzgerald, *Healthy Gains in First-Quarter Ad Spending; Nielsen: TV is up 9 Percent to \$18.77 Billion*, MEDIA LIFE MAG. (June 13, 2011), <http://www.medialifemagazine.com/Healthy-gains-in-first-quarter-ad-spending> (reporting that in the first quarter of 2011 the automotive industry spent \$2.7 billion on advertising while fast food restaurants spent \$1.1 billion and the pharmaceutical industry spent \$1 billion).

²⁰ See INV. CO. INST., 2012 INVESTMENT COMPANY FACT BOOK 108 (52d ed. 2012), available at http://www.ici.org/pdf/2012_factbook.pdf. For an overview of data for employer-sponsored plans see Craig Copeland, *Employment-Based Retirement Plan Participation: Geographic Differences and Trends, 2010*, EBRI ISSUE BRIEF 1 (Oct. 2011), available at http://www.ebri.org/pdf/briefspdf/EBRI_IB_10-2011_No363_Ret_Part.pdf (finding that 54.2% of full-time salaried employees worked for an employer that sponsored a retirement plan and 54.4% of those workers participated).

²¹ See INV. CO. INST., *supra* note 20, at 106. This phenomenon has sparked calls for increased regulation of intermediaries. See, e.g., Jill E. Fisch, *Rethinking the Regulation of Securities Intermediaries*, 158 U. PA. L. REV. 1961 (2010).

²² See Light, *supra* note 12 (noting that almost 20% of Americans over sixty-five take ten or more medications weekly).

²³ See, e.g., Donald C. Langevoort, *The SEC, Retail Investors, and the Institutionalization of the Securities Markets*, 95 VA. L. REV. 1025, 1025 (2009) (“[T]hroughout the SEC’s history and culture, the rhetorical stress has been on the plight of average investors, ones who lack investing experience and sophistication so as to need the protection of the securities laws.”).

²⁴ Studies have shown that patients fail to understand the risks and benefits associated with medical treatment. See, e.g., David A. Hertz et al., *Informed Consent: Is it a Myth?*, 30 NEUROSURGERY 453 (1992); Margaret L. Schwarze et al., *Exploring Patient Preferences for Infrainguinal Bypass Operation*, 202 J. AM. C. SURGEONS 445 (2006).

²⁵ Section 917 of the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 charged the SEC with identifying the existing level of financial literacy of retail investors. In response, the SEC’s Office of Investor Education and Advocacy commissioned a study. Pub. L. No. 111-203, 124 Stat. 1376 (2010). The study’s results suggested that the majority of retail investors do not understand basic and critical financial concepts, such as compound interest, inflation, diversification, or even the difference between stocks and bonds. See U.S. SEC. & EXCH. COMM’N, *STUDY REGARDING FINANCIAL LITERACY AMONG INVESTORS* iii-iv (2012), available at <http://www.sec.gov/news/studies/2012/917-financial-literacy-study-part1.pdf>.

protecting the average citizen are complicated even further by a layer of sophisticated players.²⁶ In the drug context, physicians are the sophisticated party. Once a drug is approved by the FDA, physicians enjoy tremendous prescribing freedom. They may prescribe the drug for an indication approved by the FDA (on-label) or to treat a condition for which the drug was not approved (off-label). Doctors rarely feel constrained by the labeled indications and routinely prescribe drugs off-label for conditions for which there is no supportive clinical data.²⁷

Similarly, in the SEC context, the “smart money” or “sophisticated investors” are comprised of institutional investors, auditors, and analysts, among others, who are seen as being able to exploit insiders’ expertise to the disadvantage of retail investors.²⁸ Thus, both agencies struggle with balancing concerns about overregulation versus protecting members of the public who may lack the knowledge and sophistication necessary to protect oneself.

Lastly, the SEC and the FDA both confront the reality that they are charged with protecting the public from an inherent risk that is largely unknown.²⁹ In the context of drug approvals, the FDA is faced with the difficult conundrum of trying to protect patient consumers from risks that are largely unascertained and will vary from patient to patient. The risks are often physical and sometimes even fatal. As Richard Merrill, former Chief Counsel to the FDA, has opined: “[a]ll consumers of

²⁶ In the financial context, the experienced institutional investors are known as “sophisticated investors.” In the drug contexts, the prescribers of drugs, typically physicians, are known as “learned intermediaries.” See, e.g., Timothy S. Hall, *Reimagining the Learned Intermediary Rule for the New Pharmaceutical Marketplace*, 35 SETON HALL L. REV. 193, 202–03 (2004) (“The prescribing physician, so the theory goes, acts as a ‘learned intermediary’ between the end user and the drug manufacturer. She is an ‘intermediary’ because a prescription drug cannot be legally obtained without a prescription from a licensed physician. She is ‘learned’ because of the extensive medical training that enables her to comprehend the content of a complete and necessarily technical and complex warning about the drug.” (footnote omitted)); Felicia Smith, *Madoff Ponzi Scheme Exposes “The Myth of the Sophisticated Investor”*, 40 U. BALT. L. REV. 215, 218 (2010) (Investors “are considered to be sophisticated investors because they have the resources and financial expertise to obtain access to, and evaluate, information concerning the offering they deem significant for their respective investment decisions and investment objectives.”).

²⁷ See Daniel B. Klein & Alexander Tabarrok, *Do Off-Label Drug Practices Argue Against FDA Efficacy Requirements? A Critical Analysis of Physicians’ Argumentation for Initial Efficacy Requirements*, 67 AM. J. ECON. & SOC. 743, 755 (2008), available at <http://econfaculty.gmu.edu/klein/PdfPapers/AJESNov2008.pdf> (“Indeed, 80 percent to 90 percent of pediatric patient regimens involved at least one off-label prescription.”); David C. Radley, Stan N. Finkelstein, & Randall S. Stafford, *Off-label Prescribing Among Office-Based Physicians*, 166 ARCHIVES INTERNAL MED. 1021, 1023 (2006), available at <http://archinte.jamanetwork.com/article.aspx?articleid=410250> (finding that 73% of off-label prescriptions lacked evidence of clinical efficacy).

²⁸ See Fisch, *supra* note 21, at 2002.

²⁹ BENGT D. FURBERG & CURT D. FURBERG, *EVALUATING CLINICAL RESEARCH: ALL THAT GLITTERS IS NOT GOLD* 8 (2d ed. 2007) (“[A]s many as half of all new drugs have at least one serious adverse effect that is unknown at the time of drug approval.”).

prescription drugs serve as guinea pigs for the pharmaceutical industry, for every new drug remains basically experimental even after it has been approved for general use.”³⁰ Annually, adverse reactions to prescription drugs cause roughly 100,000 deaths.³¹ Each year, roughly three times as many people die of adverse reactions to prescription drugs than in car accidents.³² Further, nearly 1.9 million hospitalizations annually are due to side effects from prescriptions or prescribing errors.³³

Similarly, the SEC encounters the same difficulties in trying to protect investors from unknown investment risks.³⁴ In the SEC context, the risks are financial. Market volatility and market crashes lead to real economic losses.³⁵ Yet, precious little is known about what actually causes markets to crash.³⁶

Although the FDA and SEC grapple with similar regulatory challenges, the agencies have charted very distinct courses. SEC regulations are largely based on a disclosure paradigm. Justice Louis Brandeis is often quoted for the proposition that sunlight is the “best of disinfectants,”³⁷ and the SEC has steadfastly embraced this belief. Disclosure and transparency are at the core of SEC regulations. The underpinnings of the SEC model reflect a belief in freedom of choice. By intentionally eschewing the role of the gatekeeper or merit-regulator, the SEC aims to provide accurate information to investors so that she

³⁰ See Richard A. Merrill, *Compensation for Prescription Drug Injuries*, 59 VA. L. REV. 1, 20 (1973) (internal quotation marks omitted).

³¹ Barkur S. Shastry, *Pharmacogenetics and the Concept of Individualized Medicine*, 6 PHARMACOGENOMICS J. 16, 16 (2006).

³² The total number of traffic fatalities was 32,367 in 2011. See *Death Rates from Guns, Traffic Accidents Converging*, USA TODAY (Jan. 9, 2013, 12:21 PM), <http://www.usatoday.com/story/news/nation/2013/01/09/guns-traffic-deaths-rates/1784595>.

³³ Kevin B. O’Reilly, *Quantifying Adverse Drug Events: Med Mishaps Send Millions Back for Care*, AM. MED. NEWS (June 13, 2011), <http://www.ama-assn.org/amednews/2011/06/13/prl20613.htm>.

³⁴ In the SEC context, volatility in the stock market is a given. See Tamar Frankel, *What Can Be Done About Stock Market Volatility?*, 69 B.U. L. REV. 991, 991 (1989) (“Volatility is as old as the financial markets.”).

³⁵ See Eugene A. Ludwig, *Assessment of Dodd-Frank Financial Regulatory Reform: Strengths, Challenges, and Opportunities for a Stronger Regulatory System*, 29 YALE J. ON REG. 181, 182 (2012). Prior to the recent financial crisis, the accounting irregularities that led to the downfall of Enron and WorldCom sent massive ripples from Wall Street to Main Street. See, e.g., Alena Allen, *State-Mandated Disability Insurance as Salve to the Consumer Bankruptcy Imbroglia*, 2011 BYU L. REV. 1327 (2011) (noting that over 7.2 million jobs have been lost since the recession began in 2007 and 1.4 million people filed for bankruptcy); David E. Rovella, *Charges Unlikely for Top Execs at Enron, WorldCom*, L.A. BUS. J., Aug. 25, 2003, at 18 (noting that corporate collapses destroyed 35,000 jobs and \$1 billion in employee pensions).

³⁶ Frank Partnoy, *Why Markets Crash and What Law Can Do About It*, 61 U. PITT. L. REV. 741, 741 (2000) (“[A]fter hundreds of market crashes, and centuries of study, we understand very little about them.” (footnote omitted)).

³⁷ See LOUIS D. BRANDEIS, *OTHER PEOPLE’S MONEY AND HOW THE BANKERS USE IT* 92 (1914) (“Publicity is justly commended as a remedy for social and industrial diseases. Sunlight is said to be the best of disinfectants; electric light the most efficient policeman.”).

may make informed decisions. The SEC is largely unconcerned with whether an investment is good or bad, sound or unsound, risky or safe. However, the SEC is concerned with whether the public had truthful information about the investment prior to deciding to invest.

In contrast, the FDA exercises its regulatory muscle primarily through its merit-based regulation. In its role as merit-regulator, the FDA purports to protect the public from unsafe and ineffective drugs. Thus, by exercising its discretion to approve or disapprove a drug, the FDA uses its subjective judgment to evaluate whether a drug “merits” approval. Interestingly, the wisdom of the SEC disclosure model has been both challenged and championed in the literature.³⁸ Yet, there are scant Articles questioning the wisdom of merit-based regulation in the drug context in spite of its many shortcomings and inefficiencies.³⁹ Thus, scholars have generally accepted the baseline proposition that the FDA should function as a market-regulator “protecting” the public from unsafe and ineffective drugs through its ability to approve drugs.⁴⁰

This Article rejects that baseline proposition because that assumption is based on a faulty premise. It is impossible to fully understand the risks or benefits of a drug before it is widely prescribed. In its current role as merit-regulator, the FDA has failed to protect the public from safe and ineffective drugs and has limited consumer access to drugs.⁴¹ The FDA’s mission is an impossible one. Thus, the proper role of the FDA, like the SEC, should be to facilitate disclosure and not to regulate merit. Additionally, the FDA should shift adequate resources into post-market surveillance so that it will be able to quickly act in the event that a marketed drug is unsafe.

Consequently, this Article proposes that the FDA abandon its merit-regulation paradigm and adopt a regulatory philosophy similar to that of the SEC, which facilitates disclosure and favors access. Before discussing the intricacies of the proposal, Part II provides a brief history of how the SEC and the FDA came into being. Part III of this Article discusses the current regulatory paths forged by each agency. In Part IV,

³⁸ See Frank H. Easterbrook & Daniel R. Fishel, *Mandatory Disclosure and the Protection of Investors*, 70 VA. L. REV. 669, 696 (1984) (“Information is costly, and the costs are borne in large part by investors. Whether investors benefit by more information depends on whether the marginal benefits of increments to knowledge exceed the marginal costs.”). *But see* John C. Coffee, Jr., *Market Failure and the Economic Case for a Mandatory Disclosure System*, 70 VA. L. REV. 717, 722 (1984) (“A mandatory disclosure system can . . . be seen as a desirable cost reduction strategy through which society, in effect, subsidizes search costs to secure both a greater quantity of information and a better testing of its accuracy.”).

³⁹ See *infra* Part IV for a detailed discussion of the failures of merit-based regulation.

⁴⁰ See, e.g., Michael J. Malinowski, *Government RX—Back to the Future in Science Funding? The Next Era in Drug Development*, 51 U. LOUISVILLE L. REV. 101 (2012) (proposing more governmental intervention in drug development); *see also* Parasidis, *supra* note 8, at 933 (noting the limitations of FDA review and how “tort law has traditionally served as a complementary means of regulating medical products”).

⁴¹ See *infra* Part IV.

this Article summarizes the inefficiencies plaguing the current merit-based drug approval paradigm. Part V proposes a disclosure-based framework as a more efficient and effective regulatory model for the FDA. Finally, Part VI of this Article offers a brief conclusion.

I. THE FDA AND SEC: A SHARED BIRTH STORY

Agencies regulate to establish order or method. The regulatory powers bestowed to the FDA and SEC are products of the tragedies from which each industry sprang. Their creation stories are similar but their evolutionary paths are quite distinct. For the FDA, the path taken by the SEC represents not only the road not taken but also the road that should have been taken. Legislation that is spawned by acute and urgent tragedy is often hasty with mixed results.

As will be discussed below, both agencies were essentially created to protect the public. To carry out its mission, the SEC's regulatory scheme requires substantial disclosure obligations and ensures compliance through criminal and civil enforcement. Central to the SEC's philosophy is the notion that the public should be protected from fraud but not from making unwise, foolish, or risky investments.

In contrast, the FDA's scheme requires that it play the role of an omniscient merit-regulator charged with keeping unsafe and ineffective drugs from ever being marketed to the public. The FDA's philosophy is paternalistic and thwarts patient self-determination and autonomy. The following brief overview of the agencies' creation stories provides some insight into why their regulatory paths diverged.

A. *Protecting the Public's Wealth*

A major catalyst for the creation of the SEC was the stock market crash of 1929. Thousands saw their wealth disappear seemingly overnight. Of the roughly \$50 billion of securities that were sold in the decade following World War I, approximately \$25 billion proved to be totally worthless.⁴² Between September 1, 1929 and July 1, 1932, the value of all the securities traded on the New York Stock Exchange

⁴² See Alan B. Levenson, *The Role of the SEC as a Consumer Protection Agency*, 27 BUS. LAW. 61, 61 (1971) ("The need for protective reform was pointed out clearly by the *House Report of the 73d Congress* which stated that 'During the post war decade some 50 billion dollars worth of new securities were floated in the United States. Fully half or 25 billion dollars worth of securities floated during this period have proven to be worthless. These cold figures spell tragedy in the lives of thousands of individuals who invested their life savings, accumulated after years of effort, in these worthless securities.'").

plummeted 83%.⁴³ The crash was either the beginning or a symptom of the Great Depression.⁴⁴ In either event, Congressional action was needed to protect the public and encourage trust in the markets.⁴⁵

When recommending the passage of the Securities Act of 1933, “[President] Roosevelt emphasized that by putting ‘the burden of telling the whole truth on the seller,’” the act would “bring back public confidence.”⁴⁶ At the heart of the Securities Act of 1933 was the requirement that corporations offering securities for sale to the public disclose basic useful information to investors and potential investors.⁴⁷ Thus, Congress enacted the Securities Act of 1933⁴⁸ (the Securities Act) and the Securities Exchange Act of 1934⁴⁹ (the Exchange Act) to “substitute a philosophy of full disclosure for the philosophy of *caveat emptor*.”⁵⁰

B. *Protecting the Public’s Health*

Similarly, the modern FDA is the child of a national tragedy. Although the FDA can trace its history back more than 150 years,⁵¹ the

⁴³ See JOEL SELIGMAN, *THE TRANSFORMATION OF WALL STREET* 1 (2d ed. 1995).

⁴⁴ The relationship between the crash and the depression has been debated by scholars. Compare SUSAN PREVIAANT LEE & PETER PASSELL, *A NEW ECONOMIC VIEW OF AMERICAN HISTORY* 372–83 (1979) (opining that a decline in consumption caused by stock market decline may have contributed to the Great Depression), with THOMAS K. MCCRAW, *PROPHETS OF REGULATION: CHARLES FRANCIS ADAMS, LOUIS D. BRANDEIS, JAMES M. LANDIS, ALFRED E. KAHN* 180 n.49 (1984) (“This connection between the crash and the depression, though valid in the minds of New Dealers, has been challenged by modern scholars.”).

⁴⁵ Although protection of the public was clearly a major goal of the new legislation, it was clearly not the only goal. See, e.g., Cynthia A. Williams, *The Securities and Exchange Commission and Corporate Social Transparency*, 112 HARV. L. REV. 1197, 1227 (1999) (“The acts were designed to reassert social control over capital that Congress thought had been used for the private benefit of relatively few people, to the detriment of millions, and had been misallocated to fuel speculation on Wall Street instead of to support the development of local businesses and agriculture.”).

⁴⁶ Joel Seligman, *The Historical Need for a Mandatory Corporate Disclosure System*, 9 J. CORP. L. 1, 51 (1983) (noting that lack of confidence in the stock market was largely responsible for the decrease in new corporate securities from \$9.4 billion in 1929 to \$380 million in 1933); see Louis Lowenstein, Essay, *Financial Transparency and Corporate Governance: You Manage What You Measure*, 96 COLUM. L. REV. 1335, 1339 (1996) (noting that the securities laws were “adopted by a Congress fearful of a loss of confidence in U.S. financial markets brought on by the Great Depression”).

⁴⁷ The Securities Act of 1933 delineated basic types of information to be disclosed and prescribed fraudulent practices. For example, the Act requires the issuer of securities to provide the investor with a statement of capitalization and information regarding the method used to determine the security’s value. 15 U.S.C. §§ 77g, 77aa (2012).

⁴⁸ 15 U.S.C. §§ 77a–77aa (2012).

⁴⁹ 15 U.S.C. §§ 78a–78pp (2012).

⁵⁰ *Sec. & Exch. Comm’n v. Capital Gains Research Bureau, Inc.*, 375 U.S. 180, 186 (1963).

⁵¹ See *Milestones in U.S. Food and Drug Law History*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/WhatWeDo/History/Milestones/ucm128305.htm> (last updated Nov. 6, 2012).

modern FDA was created by the Federal Food, Drug, and Cosmetic Act (FDCA) of 1938,⁵² after public confidence in drugs and elixirs was shattered. Prior to enactment of the FDCA, the Pure Food and Drugs Act of 1906 was the major legislative effort that empowered the FDA.⁵³ The 1906 Act was extremely limited in scope and was mainly concerned with the labeling of drugs. Under the 1906 Act, a drug product was deemed misbranded only if the labeling contained false or misleading information about its ingredients.⁵⁴ Thus, the 1906 Act empowered the FDA to act when the public was misled regarding ingredients, but not with respect to product claims. The FDA also lacked the power to require any safety tests prior to marketing.⁵⁵

In sum, the 1906 Act did not empower the FDA to protect the public from harmful drugs. The regulatory holes in the 1906 Act became readily apparent after the sulfanilamide incident, which made headlines across America in 1937.⁵⁶ During that period, sulfanilamide, a drug used to treat streptococcal infections, had been safely prescribed for years in tablets and powdered form.⁵⁷ However, a liquid version of the drug was needed, especially for children. In an effort to capitalize on the unmet demand, the chief chemist and pharmacist for S.E. Massengill Company began conducting experiments and soon discovered that sulfanilamide would dissolve in diethylene glycol.⁵⁸ The chemist, however, was not aware of the fact that diethylene glycol is a highly toxic substance.⁵⁹

Tragically, the 1906 Act did not require, nor did the chemist decide to conduct, safety testing prior to distribution. Thus, the chemist only tested for flavor, appearance, and fragrance before shipping hundreds of

⁵² Act of June 30, 1906, Pub. L. No. 59-384, 34 Stat. 768, *repealed by* Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717, 52 Stat. 1040 (codified as amended at 21 U.S.C. §§ 301–399(d) (2012)).

⁵³ 34 Stat. 768; *see also* U.S. FOOD & DRUG ADMIN., *supra* note 51 (noting that “cure-all claims for worthless and dangerous patent medicines” lead to the enactment of the 1906 Act).

⁵⁴ § 8, 34 Stat. at 770 (“[T]he term ‘misbranded’ . . . shall apply to all drugs, or articles of food, or articles which enter into the composition of food, the package or label of which shall bear any statement, design, or device regarding such article, or the ingredients or substances contained therein which shall be false or misleading in any particular, and to any food or drug product which is falsely branded as to the State, Territory, or country in which it is manufactured or produced.”).

⁵⁵ *See generally* DRUG APPROVAL REPORT, *supra* note 11, at 3.

⁵⁶ *See* Katharine A. Van Tassel, *Slaying the Hydra: The History of Quack Medicine, the Obesity Epidemic and the FDA’s Battle to Regulate Dietary Supplements Marketed as Weight Loss Aids*, 6 IND. HEALTH L. REV. 203, 223–24 (2009) (“It took the Elixir Sulfanilamide crisis of 1937, when over 100 people died—mostly children—to finally trigger the passage of a law to provide the FDA with the tools to begin its fight against quack medications.”).

⁵⁷ *See* Carol Ballentine, *Taste of Raspberries, Taste of Death: The 1937 Elixir Sulfanilamide Incident*, U.S. FOOD & DRUG ADMIN. (June 1981), <http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SulfanilamideDisaster/default.htm>.

⁵⁸ *Id.*

⁵⁹ *See* Arthur Hull Hayes, *Food and Drug Regulation After 75 Years*, 246 JAMA 1223, 1224 (1981) (noting that diethylene glycol is highly toxic and commonly used in anti-freeze).

boxes of the new formulation.⁶⁰ Doctors immediately began prescribing the new formulation and more than one hundred people across the country died before S.E. Massengill and the FDA realized that the addition of diethylene glycol made the “elixir” toxic to humans.⁶¹ When the FDA realized the toxicity of the “elixir,” it began seizing shipments.⁶² Ironically, the FDA was empowered to seize the product under the 1906 Act not because of toxicity of the drug or lack of pre-market safety testing, but because the drug was misbranded. The term “elixir” on the label of the drug implied that the product was an alcohol-based solution, when it did not in fact contain a drop of alcohol.⁶³

The deaths were widely reported and sparked public outcry. In 1938, Congress reacted to the sulfanilamide crisis by repealing the 1906 Act and replacing it with the FDCA.⁶⁴ The FDCA sought to close many of the regulatory gaps contained in the 1906 Act and restore public confidence in drugs. Most notably, the FDCA strengthened drug regulations by: (1) prohibiting interstate sales of new drugs unless manufacturers furnished scientific proof to the FDA of the new products’ safety prior to marketing; (2) providing the FDA with specific authority to inspect manufacturing facilities; (3) authorizing federal courts to restrain violations of the Act through injunctions; (4) eliminating proof of fraud as a requirement to enjoin false claims for drugs; and (5) requiring labels of drugs to include directions for use and to warn of special properties or hazards associated with the use of the drug.⁶⁵

Although, the FDCA was amended in 1948⁶⁶ and 1951,⁶⁷ the framework of the original 1938 version was largely undisturbed. In

⁶⁰ See Ballentine, *supra* note 57.

⁶¹ Sadly, many children, who could not swallow tablets, were prescribed the elixir. The victims exhibited symptoms including cessation of urination, severe abdominal pain, nausea, vomiting, stupor, and convulsions.

In a letter to President Franklin D. Roosevelt, a woman described the death of her child: “The first time I ever had occasion to call in a doctor for [Joan] and she was given Elixir of Sulfanilamide. All that is left to us is the caring for her little grave. Even the memory of her is mixed with sorrow for we can see her little body tossing to and fro and hear that little voice screaming with pain and it seems as though it would drive me insane. . . . It is my plea that you will take steps to prevent such sales of drugs that will take little lives and leave such suffering behind and such a bleak outlook on the future as I have tonight.”

Ballentine, *supra* note 57 (alterations in original); see Hayes, *supra* note 59, at 1223–24.

⁶² See Hayes, *supra* note 59.

⁶³ See Ballentine, *supra* note 57.

⁶⁴ Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717, 52 Stat. 1040 (codified as amended at 21 U.S.C. §§ 301–399(d) (2012)).

⁶⁵ DRUG APPROVAL REPORT, *supra* note 11, at 3.

⁶⁶ The 1948 Amendment, known as the Miller Amendment, clearly gave the FDA jurisdiction over drugs and other products that became adulterated or misbranded after interstate shipment and at all levels of the distribution chain. Act of June 24, 1948, Pub. L. No.

many respects, the FDA and SEC shared similar paths until 1962. The 1938 version of the FDCA protected the public by requiring that manufacturers disclose evidence of safety prior to marketing without authorizing the FDA to interject a subject risk-benefit assessment of the drug. Thus, the original FDA paradigm was largely akin to the SEC's model. The focus was on accurately disclosing and preventing fraud.

II. THE FDA AND SEC: SHARED MISSION, DIFFERING PATHS

The SEC and the FDA not only share a similar birth story, but they also share the mission of protecting a relatively unsophisticated public.⁶⁸ While the challenges facing these kindred agencies are similar, the paths taken by the agencies are remarkably divergent. This section illuminates how the agencies evolved on divergent paths.

A. *The SEC's Road to Disclosure*

The notion of “merit review” of securities was not a novel concept in the early 1900s.⁶⁹ In 1911, the state of Kansas enacted the first “blue sky” laws.⁷⁰ The laws required that anyone selling securities in Kansas must first receive a permit from the state's bank commissioner and file regular reports regarding financial conditions. The bank commissioner was vested with the discretion not to issue a permit if he did not approve

80-749, 62 Stat. 582 (codified as amended at 21 U.S.C. §§ 331(a), (k) (2012)); see DRUG APPROVAL REPORT, *supra* note 11, at 5–6.

⁶⁷ The Durham-Humphrey Amendment of 1951 clearly delineated what types of drugs may not be sold or refilled without a prescriber's authorization. The amendments left discretion to the states to determine who is qualified to prescribe drugs. Act of Oct. 26, 1951, Pub. L. No. 82-215, 65 Stat. 648 (codified as amended at 21 U.S.C. §§ 303(c), 503(b) (2012)); DRUG APPROVAL REPORT, *supra* note 11, at 6.

⁶⁸ See *supra* note 9 and accompanying text.

⁶⁹ Merit review of regulation refers to the sagacity of state securities commissioners to make qualitative assessments regarding the merits of an offering or sale of securities in the state. See, e.g., Gregory Gorder, *Compromise Merit Review—A Proposal for Both Sides of the Debate*, 60 WASH. L. REV. 141 (1984); Roberta S. Karmel, *Blue-Sky Merit Regulation: Benefit to Investors or Burden on Commerce?*, 53 BROOK. L. REV. 105 (1987).

⁷⁰ “Blue sky” laws were apparently given that moniker because their purpose was to thwart charlatans who would “sell building lots in the blue sky in fee simple.” Thomas Mulvey, *Blue Sky Law*, 36 CAN. L. TIMES 37, 37 (1916). Although this account has been repeated many times, some scholars have called its accuracy into question. See, e.g., Jonathan R. Macey & Geoffrey P. Miller, *Origin of the Blue Sky Laws*, 70 TEX. L. REV. 347, 350 (1991) (“[A]lthough fraudulent securities undoubtedly occurred during the early decades of the century, the standard account that securities fraud was rampant before the advent of blue sky regulation is not proven.”); Paul G. Mahoney, *The Origins of the Blue-Sky Laws: A Test of Competing Hypotheses*, 46 J.L. & ECON. 229, 249 (2003) (finding “no evidence that the statutes responded to actual instances of fraud”).

of the merits of the offering.⁷¹ Twenty years later, forty-seven of the forty-eight states had adopted statutes regulating securities.⁷²

Not surprisingly, the original draft of the Securities Act contemplated merit review. For example, it granted the SEC broad powers of discretion to revoke an issuer's registration after finding that the "business of the issuer, or person, or the security is not based upon sound principles, and that the revocation is in the interest of the public welfare."⁷³ However, federal merit-regulation failed to garner the support of President Roosevelt, who did not view the federal government's role as "approving or guaranteeing" the soundness of securities.⁷⁴

Instead, President Roosevelt viewed the government's role as ensuring honesty and fair dealing in the selling of securities.⁷⁵ Roosevelt sold his vision to Congress, which adopted a mandatory disclosure system, and left merit-regulation to the discretion of the states.⁷⁶ Thus, the modern federal regulatory paradigm is based not on merit-regulation, but instead on disclosure.⁷⁷ There are four broad categories

⁷¹ The commissioner could deny a permit if the offering contained provisions that were "unfair, unjust, inequitable or oppressive to any class of contributors" or if the company was "not solvent and [did] not intend to do a fair and honest business." In addition, the commissioner could deny a permit if in his judgment the offering did not "promise a fair return." See Act of March 10, 1911, ch. 133, § 5, 1911 Kan. Sess. Laws 210.

⁷² See Mahoney, *supra* note 70, at 229.

⁷³ S. 875 & H.R. 4314, 73d Cong. 1st Sess. § 6(f) (1933), reprinted in 3 LEGISLATIVE HISTORY OF THE SECURITIES ACT OF 1933 AND SECURITIES EXCHANGE ACT OF 1934 (J. S. Ellenberger & Ellen P. Mahar eds., 2001). In addition, the original draft provided for revocation where the issuer was financially unsound or insolvent. See *id.*, §§ 6(c), (e), (f).

⁷⁴ 77 CONG. REC. 937 (1933).

⁷⁵ *Id.* (message from Franklin D. Roosevelt to the Senate, Mar. 29, 1933, introducing legislation that became the Securities Act of 1933) ("In spite of many State statutes the public in the past has sustained severe losses through practices neither ethical nor honest on the part of many persons and corporations selling securities. . . . There is . . . an obligation upon us to insist that every issue of new securities to be sold in interstate commerce shall be accompanied by full publicity and information, and that no essentially important element attending the issue shall be concealed from the buying public.").

⁷⁶ The Securities Act provided that "[n]othing in this title shall affect the jurisdiction of the securities commission . . . of any State or Territory of the United States, or the District of Columbia, over any security or any person." Securities Act of 1933, Pub. L. No. 73-22, § 18, 48 Stat. 74 (codified as amended at 15 U.S.C. § 77r (2012)).

⁷⁷ See Michael H. Sutton, Chief Accountant U.S. Sec. & Exch. Comm'n, International Harmonization of Accounting Standards: Perspectives from the Securities and Exchange Commission, Remarks at the American Accounting Association Annual Meeting (Aug. 17, 1997), available at 1997 WL 486335 (S.E.C.), at *3 ("In US capital markets, investor protection is achieved not through merit regulation—allowing only healthy companies to trade their securities—but by market regulation—ensuring that all who seek access to US markets provide full and fair disclosure of the risks to investors."). Disclosure regulation continues to be favored by Congress and the SEC. For example, after the collapse of Enron and WorldCom, the SEC proposed adding eleven new items to the 8-K. See Additional Form 8-K Disclosure Requirements and Acceleration of Filing Date, Exchange Act Release No. 34-46,084, 77 SEC Docket 2579 (proposed June 17, 2002), available at 2002 WL 1315511. In addition, the SEC added new requirements for reporting of certain insider transactions and loans. Form 8-K

of disclosure required: (1) initial disclosure when securities are first issued to the public;⁷⁸ (2) periodic reporting consisting of disclosures when registered and then quarterly and annually thereafter;⁷⁹ (3) proxy disclosures in conjunction with elections at the annual shareholders' meeting;⁸⁰ and (4) disclosures associated with extraordinary corporate events.⁸¹

Disclosure is the bedrock of securities regulation. The notion that disclosure is the remedy for almost any market malaise is rooted in the law and economics movement.⁸² Gary Becker's work succinctly explains the key principles: "[A]ll human behavior can be viewed as involving participants who [1] maximize their utility [2] from a stable set of preferences and [3] accumulate an optimal amount of information and

Disclosure of Certain Management Transactions, Exchange Act Release No. 34-45,742, 77 SEC Docket 1072 (proposed Apr. 12, 2002), *available at* 2002 WL 538909.

⁷⁸ Securities Act §§ 5, 7, 10, sched. A–B (codified as amended at 15 U.S.C. §§ 77e, 77g, 77j, 77aa (2012)).

⁷⁹ Securities Exchange Act of 1934, Pub. L. No. 73-291, §§ 12(b)(1), 13, 15(d), 48 Stat. 881 (codified as amended at 15 U.S.C. §§ 78l(b)(1), 78l(g)(1), 78m, 78o(d) (2012)).

⁸⁰ Securities Act § 14 (codified as amended at 15 U.S.C. § 78n (2012)).

⁸¹ *Id.* §§ 14(a), (d), (f) (codified as amended at 15 U.S.C. §§ 78n(a), (d), (f) (2012)).

⁸² At its core, law and economics is the analysis of legal rules using basic economic principles. The field of law and economics was in many ways pioneered by Gary Becker, Guido Calabresi, and Ronald Coase during the 1960's. See Gary S. Becker, *Crime and Punishment: An Economic Approach*, 76 J. POL. ECON. 169 (1968) (applying economic analysis to criminal behavior in an attempt to develop optimal strategies to combat illegal activity by viewing the criminal as a rational actor and weighing the benefits of committing a given crime against the consequences of being caught and ultimately punished); Guido Calabresi, *Some Thoughts on Risk Distribution and the Law of Torts*, 70 YALE L.J. 499 (1961) (analyzing the economic logic of tort law); Ronald H. Coase, *The Problem of Social Cost*, 3 J.L. & ECON. 1 (1960), *available at* http://grecof2.econ.univpm.it/esposti/wiki/lib/exe/fetch.php?media=didattica:coase_jle1960.pdf. Coase's Article offered a framework for analyzing the assignment of property rights and liability in economic terms. Coase's work was expanded upon by Calabresi and Melamed in another highly influential work. See Guido Calabresi & A. Douglas Melamed, *Property Rules, Liability Rules, and Inalienability: One View of the Cathedral*, 85 HARV. L. REV. 1089 (1972) (using law and economics analysis to construct a framework for viewing the legal relationships in property and tort law from a "unified perspective"). However, some scholars viewed Coase's central contribution more broadly. For example, Jennifer Arlen noted that that a central contribution of Coase's work was the claim that one cannot determine the effect of a law by simply looking at the law itself, and that instead one must determine how individuals will respond to the law. Jennifer Arlen, *Comment: The Future of Behavioral Economic Analysis of Law*, 51 VAND. L. REV. 1765, 1765–66 (1998) (noting the central importance of Coase's work and the link between traditional law and economics analysis and modern behavioral economic analysis of law). Prior to their work, the field of law and economics was limited almost exclusively in application to antitrust laws. See, e.g., Richard A. Posner, *The Economic Approach to Law*, 53 TEX. L. REV. 757, 758 (1975) ("[T]he application of economics to antitrust has never been particularly controversial among economists. Even among academic lawyers, the appropriateness of placing economics in the foreground of antitrust analysis has been generally accepted."); see also Joseph F. Brodley, *The Economic Goals of Antitrust: Efficiency, Consumer Welfare, and Technological Progress*, 62 N.Y.U. L. REV. 1020, 1020 (1987) (acknowledging the ascendancy of economic efficiency analysis in the area of antitrust law).

other inputs in a variety of markets.”⁸³ Simply stated, the basis of the law and economics field is the assumption that individuals behave rationally⁸⁴ and that rational actors act to maximize their preferences.⁸⁵ This basic assumption is drawn from neoclassical microeconomic theory.⁸⁶

Modern economic theory is at the core of the SEC’s regulatory paradigm. In the securities context, the rational maximizer hypothesis, along with the Efficient Capital Market Hypothesis (ECMH), are the pillars on which almost all regulations are based. The basic premise of EMH is that “prices at any time ‘fully reflect’ all available information.”⁸⁷ In the most general of terms, the market is efficient when the prices of traded securities accurately and quickly reflect the security’s intrinsic values relative to all publicly available information. In essence, the ECMH assumes that investors rationally respond to information that is presented. This simple hypothesis has spawned a voluminous amount of

⁸³ GARY S. BECKER, *THE ECONOMIC APPROACH TO HUMAN BEHAVIOR* 14 (1976); see also Richard A. Posner, *Values and Consequences: An Introduction to Economic Analysis of Law*, in CHICAGO LECTURES IN LAW AND ECONOMICS 189, 191 (Eric A. Posner ed., 2000) (“Most economic analysis consists of tracing out the consequences of assuming that people are more or less rational in their social interactions.”).

⁸⁴ The literature is filled with references to this basic principal. See, e.g., PAUL HEYNE, *THE ECONOMIC WAY OF THINKING* 2 (2d ed. 1976) (noting that the rational actor model is “basically a way of thinking” and that economics assumes that everyone “acts in accordance with that rule: miser or spendthrift, saint or sinner, consumer or seller, politician or business executive, cautious calculator or spontaneous improviser”); NICHOLAS MERCURO & STEVEN G. MEDEMA, *ECONOMICS AND THE LAW: FROM POSNER TO POST-MODERNISM* 57 (1997) (“[I]ndividuals are rational maximizers of their satisfactions in their nonmarket as well as their market behavior”); RICHARD A. POSNER, *ECONOMIC ANALYSIS OF LAW* 3 (5th ed. 1998) (“The task of economics . . . is to explore the implications of assuming that man is a rational maximizer of his ends in life” (footnote omitted)); Andrew Brod, *Economics as One of the Humanities: A Comment*, 4 S. CAL. INTERDISC. L.J. 313, 314 (1995) (“To economists, an economic actor, or agent, is rational if she can be construed to act as if she maximizes her utility.”); Posner, *The Economic Approach to Law*, *supra* note 82, at 761 (“The basis of an economic approach to law is the assumption that the people involved with the legal system act as rational maximizers of their satisfactions.”).

⁸⁵ For a succinct overview of the traditional model of preferences see Matthew D. Adler, Claire Finklestein, & Peter H. Huang, *Preferences and Rational Choice: New Perspectives and Legal Implications*, 151 U. PA. L. REV. 707, 708 (2003) (“[P]references must conform to the following three criteria: (1) completeness—an agent must be able to rank any two items with which she is presented, unless she is indifferent between the two; (2) transitivity—if an agent would prefer an apple to an orange, and an orange to a banana, then it must be the case that she would prefer an apple over a banana; and (3) reflexivity—an agent must be indifferent between an item and an identical item. An agent whose choices do not conform to these conditions would be thought irrational, and her preferences could not be coherently maximized.”).

⁸⁶ See generally Posner, *Values and Consequences: An Introduction to Economic Analysis of Law*, *supra* note 83.

⁸⁷ Eugene F. Fama, *Efficient Capital Markets: A Review of Theory and Empirical Work*, 25 J. FIN. 383, 383 (1970), available at <http://efinance.org.cn/cn/fm/Efficient%20Capital%20Markets%20A%20Review%20of%20Theory%20and%20Empirical%20Work.pdf>; see Louis Lowenstein, *Efficient Market Theory: Let the Punishment Fit the Crime*, 51 WASH. & LEE L. REV. 925, 926 (1994) (describing stock pricing according to EMH).

literature⁸⁸ and served as the basis for modern securities regulation⁸⁹ and litigation.⁹⁰

Operating under the assumption that investors are rational and that capital markets are efficient, Congress and the SEC have relied on disclosure regulations as the primary vehicle for protecting investors.⁹¹ A disclosure-based system of regulation has several rationales. First, requiring disclosure can induce corporate officers to behave more ethically and honestly because they know that their actions will regularly be reviewed and exposed.⁹² Second, disclosure requirements can reduce agency costs. Mandating disclosure reduces the costs that shareholders would otherwise bear in trying to monitor their agent directors and

⁸⁸ See, e.g., Daniel R. Fischel, *Efficient Capital Market Theory, the Market for Corporate Control, and the Regulation of Cash Tender Offers*, 57 TEX. L. REV. 1 (1978); Ronald J. Gilson & Reinier H. Kraakman, *The Mechanisms of Market Efficiency*, 70 VA. L. REV. 549 (1984); David M. Grether et al., *The Irrelevance of Information Overload: An Analysis of Search and Disclosure*, 59 S. CAL. L. REV. 277 (1986); Donald C. Langevoort, *Theories, Assumptions, and Securities Regulation: Market Efficiency Revisited*, 140 U. PA. L. REV. 851 (1992) (discussing how EMH has developed into intellectual orthodoxy in spite of attacks about conventional assumptions of rationality); Peter Talosig III, *Regulation FD—Fairly Disruptive? An Increase in Capital Market Inefficiency*, 9 FORDHAM J. CORP. & FIN. L. 637 (2004).

⁸⁹ For example, the SEC referenced EMH in a release: “[T]he concept of integration also proceeds from the observation that information is regularly being furnished to the market through periodic reports under the Exchange Act. . . . To the extent that the market accordingly acts efficiently . . . there seems little need to reiterate this information in a prospectus” Proposed Comprehensive Revision to System for Registration of Securities Offerings, Securities Act Release No. 6235, Investment Company Act Release No. 11,327 [1980 Transfer Binder] Fed. Sec. L. Rep. (CCH) ¶ 82,649, at 83,484 (proposed Sept. 2, 1980), available at 1980 WL 20867, at *3.

⁹⁰ EHM serves as the basis of the fraud-on-the-market theory that the Supreme Court established as a rebuttable presumption of liability for the majority of securities fraud cases. In effect, under Supreme Court jurisprudence, if the securities at issue traded in an efficient market, then reliance is presumed. In *Basic Inc. v. Levinson*, 485 U.S. 224 (1988), the Supreme Court stated that in order to invoke the fraud-on-the-market theory, the plaintiff must show: (1) defendants made public misrepresentations; (2) the misrepresentations were material (a reasonable investor would misvalue the stock); (3) shares traded in an efficient market; and (4) plaintiff traded between the time the misrepresentations were made and the truth was revealed. *Id.* at 248, 248 n.27.

⁹¹ See, e.g., *Creswell-Keith, Inc. v. Willingham*, 264 F.2d 76, 81 (8th Cir. 1959) (noting that the objective of the Securities Act is to ensure “full and fair disclosure of [the character of] securities sold in interstate and foreign commerce and through the mails, and to prevent frauds in the sale thereof” (quoting the Securities Act of 1933, Pub. L. No. 73-22, 48 Stat. 74) (internal quotation marks omitted)); Stephen J. Choi & A.C. Pritchard, *Behavioral Economics and the SEC*, 56 STAN. L. REV. 1 (2003) (noting that disclosure is the prevailing regulatory strategy in the securities markets); Rodrigues & Stegemoller, *supra* note 8, at 11 (“The principle of mandatory disclosure—to ensure equal access to information—is fundamental to our securities law.”).

⁹² See David A. Skeel, Jr., *Shaming in Corporate Law*, 149 U. PA. L. REV. 1811, 1857 (“In short, a firm that is required to disclose misbehavior may not engage in it in the first instance.”).

corporate officers.⁹³ Third, disclosure facilitates informed decision-making about whether to buy or sell a particular security, which makes the price of the security more accurate.⁹⁴ Similarly, disclosing information narrows the informational asymmetry between corporations and their officers and investors.⁹⁵ Fourth, disclosure serves the twin goals of maintaining (and at times increasing) investor confidence in the market and promoting the public good.⁹⁶

B. *The FDA's Road to Merit Review*

In contrast to the SEC, the modern FDA regulates merit. Under the 1906 law, the FDA had virtually no authority to review a drug pre-market.⁹⁷ The 1938 Act created what can be considered a disclosure-based paradigm. A drug manufacturer was obligated to disclose safety information regarding the drug when submitting a new drug

⁹³ See Paul G. Mahoney, *Mandatory Disclosure as a Solution to Agency Problems*, 62 U. CHI. L. REV. 1047, 1048–51 (1995) (noting that the purpose of disclosure laws was to help shareholders to monitor officers' self-interested and opportunistic behaviors).

⁹⁴ See Choi & Pritchard, *supra* note 91, at 22 (“[D]isclosure may assist rational investors in allocating their investment dollars, leading to better use of capital and more accurate securities prices.”); Edmund W. Kitch, *The Theory and Practice of Securities Disclosure*, 61 BROOK. L. REV. 763, 764 (1995) (“The dominant view is that the goal of required securities disclosure is to make prices in securities markets more accurate.”); Donald C. Langevoort, *Managing the “Expectations Gap” in Investor Protection: The SEC and the Post-Enron Reform Agenda*, 48 VILL. L. REV. 1139, 1152 (2003) (noting that one purpose of disclosure regulation “is to allow investors to make informed valuation decisions—in other words, what are the securities worth compared to their current price?”).

⁹⁵ See Troy A. Paredes, *Blinded by the Light: Information Overload and its Consequences for Securities Regulation*, 81 WASH. U. L.Q. 417, 418 (2003) (“The logic is that by arming investors with information, mandatory disclosure promotes informed investor decision making, capital market integrity, and capital market efficiency. Once they are empowered with information, the argument goes, investors can protect themselves against corporate abuses and mismanagement, and there is no need for the government to engage in more substantive securities regulation . . .”).

⁹⁶ See Merritt B. Fox, *Retaining Mandatory Securities Disclosure: Why Issuer Choice is Not Investor Empowerment*, 85 VA. L. REV. 1335, 1338 (1999) (“More information about the issuer and the resulting increase in its share price accuracy produces social benefits in the form of improved selection of new investment projects, improved managerial performance, and reduced investor risk.”); Marc I. Steinberg, *Curtailing Investor Protection Under the Securities Laws: Good for the Economy?*, 55 SMU L. REV. 347, 354 (2002) (contending that without investor confidence, the markets would experience a liquidity crunch, and investors would flee to other investment vehicles). To be sure, the disclosure paradigm of the SEC is not without its critics. For instance, one oft cited criticism is that people simply do not read the mandated disclosures. Many have opined that the average investor does not read let alone understand and comprehend the disclosures that are provided. See, e.g., Melvin Aron Eisenberg, *Text Anxiety*, 59 S. CAL. L. REV. 305, 309 (1986) (finding that consumers who are faced with dense and complex information that they perceive as being difficult to understand chose not to try to process the information at all and avoid the anxiety and emotional frustration). However, this Article contends that given the failings of merit-based regulation in drug approvals that a disclosure-based paradigm should be considered and debated.

⁹⁷ See discussion of the Pure Food and Drug Act, *supra* Part I.B.

application. The FDA had the authority to reject an application if it did not deem the drug safe for its intended use; however, if the FDA failed to act within sixty days, the drug was deemed approved.⁹⁸

This paradigm changed dramatically with the passage of the 1962 Amendments.⁹⁹ After 1962, the Kefauver-Harris Amendments placed the burden on the manufacturer to establish, with substantial evidence,¹⁰⁰ that the new drug was safe and effective prior to marketing.¹⁰¹ In addition, the FDA was given the authority to evaluate the efficacy of all drugs approved between 1938 and 1962 and, more importantly, the power to withdraw ineffective drugs from the market. The Kefauver-Harris Amendments also required manufactures to report adverse events to the FDA.¹⁰²

Post 1962, the FDA became the ultimate merit-regulator, having the power to question, scrutinize, and weigh the clinical utility of drugs in ascertaining whether a drug is worthy of approval. Generally, to merit approval, a manufacturer must demonstrate (1) that the drug is safe and effective for the use in the proposed labeling; and (2) that the benefits of the drug outweigh its risks.¹⁰³ In order to garner FDA approval, a drug sponsor must substantiate its claims that the drug meets this standard through the use of studies involving human research subjects, which are typically referred to as clinical trials.¹⁰⁴ The FDA collaborated with the

⁹⁸ Approval of new drugs became effective automatically after sixty days, unless the FDA elected to extend the review to 180 days from the date of filing and notified the drug sponsor. Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717, § 505(c), 52 Stat. 1040, 1052 (codified as amended at 21 U.S.C. § 355 (2012)).

⁹⁹ Perhaps the Kefauver-Harris Amendments were more sweeping in nature because like the 1938 Act, the Kefauver-Harris Amendments were born of tragedy. At the time, pregnant women were prescribed thalidomide as a sedative, but it was later discovered that the drug caused birth defects. While the drug was approved in Europe where it caused many birth defects, in the United States, the drug was prescribed on an experimental basis and linked to only nine birth defects. Still, the Amendments were enacted following and in response to these deaths. See DRUG APPROVAL REPORT, *supra* note 11, at 8.

¹⁰⁰ See Drug Amendments of 1962, Pub. L. No. 87-781, § 102, 76 Stat. 780, 781 (“[Defining] ‘substantial evidence’ [as] evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have . . .”).

¹⁰¹ 21 U.S.C. §§ 355(a)–(d) (2012).

¹⁰² *Id.* §§ 355(j), (l).

¹⁰³ See COMM. ON IDENTIFYING & PREVENTING MEDICATION ERRORS, BD. ON HEALTH CARE SERVS., INST. OF MED. OF THE NAT’L ACADS., PREVENTING MEDICATION ERRORS 58 (Philip Aspden et al. eds., 2007) [hereinafter IOM, PREVENTING MEDICATION ERRORS], available at http://books.nap.edu/openbook.php?record_id=11623.

¹⁰⁴ See *Inside Clinical Trials: Testing Medical Products in People*, FDA.GOV, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143531.htm> (last updated Apr. 12, 2013) (explaining that clinical trials are medical studies that test potential treatments in human research participants to determine whether the treatment should be released for widespread consumer use).

pharmaceutical industry and clinical researchers to create standards for testing drugs, and in 1970 issued regulations for conducting clinical trials.¹⁰⁵ The modern clinical trial process is credited with driving up the costs associated with developing new drugs¹⁰⁶ and creating an entirely new industry: the Contract Research Organization (CRO) market.¹⁰⁷

Before human clinical trials can begin, the pharmaceutical sponsor must complete preclinical testing, including animal testing.¹⁰⁸ For every 5,000 to 10,000 compounds that enter preclinical testing,¹⁰⁹ only one is expected to ultimately be approved by the FDA.¹¹⁰ If the laboratory testing in animal yields favorable results,¹¹¹ the drug manufacturer must file an Investigational New Drug (IND) Application, a request for FDA

¹⁰⁵ Hearing Regulations and Regulations Describing Scientific Content of Adequate and Well-Controlled Clinical Investigations, 35 Fed. Reg. 7250-02 (May 8, 1970) (codified at 21 C.F.R. §§ 130, 146 (2012)).

¹⁰⁶ See Christopher P. Adams & Van V. Brantner, *Estimating the Cost of New Drug Development: Is It Really \$802 Million?*, 25 HEALTH AFFAIRS 420 (2006), available at <http://content.healthaffairs.org/content/25/2/420.full.pdf+html> (estimating that drug development costs range from \$500 million to more than \$2 billion depending on the therapy or the developing firm); Joseph A. DiMasi, Ronald W. Hansen & Henry G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003), available at http://moglen.law.columbia.edu/twiki/pub/LawNetSoc/BahradSokhansanjFirstPaper/22JHealthEcon151_drug_development_costs_2003.pdf (finding the estimated average out-of-pocket cost per new drug is \$403 million); Barry S. Roberts & David Z. Bodenheimer, *The Drug Amendments of 1962: The Anatomy of a Regulatory Failure*, 1982 ARIZ. ST. L.J. 581, 606 (1982) (“Between 1962 and 1980, the cost to develop a new drug rose from \$6.5 million to \$70 million.” (footnote omitted)).

¹⁰⁷ A Contract Research Organization (CRO) is an entity that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, e.g., design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the Food and Drug Administration. Recent estimates suggest that the CRO market is roughly \$24 billion and growing by 15% per year. See Maysoun Dimachkie Masri et al., *Contract Research Organizations: An Industry Analysis*, 6 INT’L J. PHARMACEUTICAL & HEALTHCARE MARKETING 336, 337 (2012), available at 5, <http://www.guidestarclinical.com/wp-content/uploads/2013/04/CONTRACT-RESEARCH-ORGANIZATIONS-AN-INDUSTRY-ANALYSIS.pdf>.

¹⁰⁸ The animal testing not only provides insight into toxicity but is also used to calibrate the starting dosage in humans. See Edmund A. Gehan, *Clinical Trials in Cancer Research*, 32 ENVTL. HEALTH PERSP. 31, 33 (1979), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1637924/pdf/envhper00477-0034.pdf> (“Studies . . . have shown that the maximum tolerated dose in [humans] was comparable to that in five animal species (mouse, rat, hamster, dog, and monkey) when dosage was expressed per unit of surface area in square meters.”).

¹⁰⁹ See 21 C.F.R. § 312.23 (2012). Pre-clinical testing can last between two and ten years depending on the type of drug. See RICHARD E. ROWBERG, CONG. RESEARCH SERV., RL30913, PHARMACEUTICAL RESEARCH AND DEVELOPMENT: A DESCRIPTION AND ANALYSIS OF THE PROCESS 14 (2001), available at <http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/RL30913.pdf>.

¹¹⁰ See Lipsky & Sharp, *supra* note 3, at 364.

¹¹¹ It is a rare event for a drug to advance past pre-clinical testing. Most potential drugs fail to demonstrate sufficient promise to enter human trials. See COMM. ON THE ASSESSMENT OF THE U.S. DRUG SAFETY SYS., BD. ON HEALTH & PUB. HEALTH PRACTICE, INST. OF MED. OF THE NAT’L ACADEMIES, THE FUTURE OF DRUG SAFETY: PROMOTING AND PROTECTING THE HEALTH OF THE PUBLIC 33 (Alina Baciú et al. eds., 2007) [hereinafter IOM, THE FUTURE OF DRUG SAFETY], available at http://www.nap.edu/openbook.php?record_id=11750&page=R1.

authorization to conduct clinical trials for an investigational drug or biological product on humans.¹¹²

The IND application consists of the preclinical data and a description of the proposed human testing.¹¹³ The FDA has thirty days from receipt of the IND to place a hold on the proposed human trials, if safety concerns exist.¹¹⁴ If the FDA declines to intervene, the drug sponsor may proceed with human clinical trials. Approval of an IND is contingent upon the drug sponsor ensuring that all agencies and institutions that conduct or fund the human clinical trials adhere to federal regulations governing the protection of human research participants, referred to as the “common rule.”¹¹⁵ Although clinical trials vary in design, most involve concurrent groups of research subjects who are randomly assigned to receive either a placebo (the control group) or the investigational drug.¹¹⁶

Pharmaceutical companies, typically with the aid of CROs, develop study protocols and oversee the studies.¹¹⁷ Spanning multiple years and many phases, the clinical trial process is extremely costly.¹¹⁸ The typical human clinical trial process usually begins with Phase I clinical

¹¹² See *Vaccines, Blood & Biologics: Information on Submitting an Investigational New Drug Application*, FDA.GOV, <http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/InvestigationalNewDrugINDorDeviceExemptionIDEPProcess/ucm094309.htm> (last updated Sept. 8, 2011).

¹¹³ It has been estimated that the average new commercial IND submission totals about 14,000 pages. See IOM, *THE FUTURE OF DRUG SAFETY*, *supra* note 111. The IND includes a protocol that provides the design and method for conducting the trial. See Gehan, *supra* note 108, at 31–32 (“The usual elements included in a protocol [in clinical trials] are (1) introduction and scientific background for the study; (2) objectives of study; (3) selection of patients; (4) design of study (including schematic diagram); (5) treatment programs; (6) procedures in event of response, no response, or toxicity; (7) required clinical and laboratory data; (8) criteria for evaluating the effect of treatment; (9) statistical considerations; (10) informed consent; (11) record forms; (12) references; (13) study chairman or responsible investigator and telephone number.”).

¹¹⁴ 21 U.S.C. § 355(i)(2) (2012).

¹¹⁵ Karen J. Maschke, *Human Research Protections: Time for Regulatory Reform?*, 38 HASTINGS CENTER REP. 19, 19–20 (2008) (noting that the FDA has two major requirements: (1) “that an institutional review board [(IRB)] review and approve [the] studies [or trials] before individuals are asked to enroll in them” and (2) “that individuals give informed consent before they participate” in a research trial).

¹¹⁶ See LAWRENCE M. FRIEDMAN ET AL., *FUNDAMENTALS OF CLINICAL TRIALS 2* (3d ed. 1998).

¹¹⁷ In any given year, roughly 10,000 clinical studies will be conducted across the country. See DIGITAL CONNECTIONS COUNCIL, COMM. FOR ECON. DEV., *HARNESSING OPENNESS TO TRANSFORM AMERICAN HEALTH CARE 14* (2008), available at <http://www.ced.org/pdf/Harnessing-Openness-to-Improve-American-Health-Care.pdf>.

¹¹⁸ Recent estimates suggest that capitalized costs of new drug development exceed \$1 billion. In addition, the clinical failure rate is about 80%, which is exceedingly high. See Steve Morgan et al., *The Cost of Drug Development: A Systematic Review*, 100 HEALTH POL’Y 4, 14–16 (2011), available at http://moglen.law.columbia.edu/twiki/pub/LawNetSoc/BahradSokhansanjFirstPaper/100HealthPoly4_cost_of_drug_development_2010.pdf.

studies.¹¹⁹ Phase I studies typically involve between 10 and 100 healthy participants and are designed to evaluate the safety of the drug and to determine the maximum safe dosage.¹²⁰ As a result, these studies typically begin with administering very low doses, which are gradually increased.¹²¹ The average Phase I trial lasts about one and a half years and costs about \$10 million.¹²²

If the results from Phase I studies are promising, the drug advances to Phase II clinical trials. However, the FDA requires pre-approval of trial progression.¹²³ Thus, sometimes sponsors are required to conduct multiple trials of the same phase if the FDA has concerns or questions about the risk-benefit profile of the drug. Nonetheless, Phase II trials typically enroll a few hundred participants who suffer from the ailment that the drug seeks to cure.¹²⁴ Phase II trials are designed to produce preliminary data on the drug's effectiveness and determine what end points to measure during Phase III trials.¹²⁵ Phase II trials usually last for about two years and cost about \$20 million.¹²⁶

Finally, if the results from Phase II warrant proceeding, with FDA approval, the drug sponsor initiates Phase III clinical trials. Phase III trials typically involve thousands of subjects across different sites and last three to five years.¹²⁷ Similar to Phase II studies, participants in this phase have been diagnosed with the illness or disorder which the drug seeks to cure or treat. The cost of Phase III trials average about \$45 million.¹²⁸ Phase III trials are designed to elicit sufficient information

¹¹⁹ Prior to Phase I trials, sometimes drug manufactures will conduct Phase Zero trials to gather preliminary pharmacokinetic (what the body does to the drugs) and pharmacodynamics (what the drug does to the body) data. See Draft Guidance for Industry, Investigators, and Reviewers: Exploratory IND Studies, 70 Fed. Reg. 19, 764-01 (Apr. 14, 2005).

¹²⁰ See 21 C.F.R. § 312.21(a) (2012) ("Phase I . . . studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness."); see also ROWBERG, *supra* note 109, at 9.

¹²¹ See Lipsky & Sharp, *supra* note 3, at 365.

¹²² See ROWBERG, *supra* note 109, at 9.

¹²³ See Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1847 (1996) ("[T]he [FDA insists] that it approve the trial progression from Phase I to Phase II and, particularly, from Phase II to Phase III, in which many more patients will be exposed to the test drug . . .").

¹²⁴ See DEP'T OF HEALTH & HUMAN SERVS., FOOD & DRUG ADMIN., CTR. FOR DRUG EVALUATION & RESEARCH, THE CDER HANDBOOK 8 (1998) [hereinafter FDA, CDER HANDBOOK], available at <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM198415.pdf>.

¹²⁵ See *id.*

¹²⁶ Generally, a clinical trial will specify a primary endpoint as a measure of what will be considered a successful therapy. Common end points include absence of the disease or statistically significant improvement in overall survival. See ROWBERG, *supra* note 109, at 10.

¹²⁷ *Id.* at 11.

¹²⁸ *Id.*

about the drug's safety and efficacy so that predictions about its effect in the general population can be made.¹²⁹

After the completion of the clinical trials, drug manufacturers wishing to procure approval must file a New Drug Application (NDA).¹³⁰ The FDA typically receives slightly more than 100 NDAs per year.¹³¹ Within the FDA, the Center for Drug Evaluation and Research (CDER) does an initial review of the NDA to determine whether it is accepted for review. CDER has sixty days in which to decide to accept or "refuse to file an application."¹³² If the FDA accepts the NDA, by statute the FDA has 180 days to review it.¹³³ In practice, the FDA review time is much longer.¹³⁴

Once an NDA has been accepted, a project manager and primary scientific reviewers are assigned.¹³⁵ Reviewers typically focus on four questions: (1) whether the drug is safe and effective for its proposed use;¹³⁶ (2) whether the drug's benefits outweigh the risks;¹³⁷ (3) whether the manufacturer's proposed labeling is appropriate and complete; and (4) whether the methods that will be used to manufacture the drug are adequate to preserve the drug's identity, strength, quality, and purity.¹³⁸

¹²⁹ In order for a drug to merit approval, in most cases the FDA requires that drug manufacturers provide at least two adequate and well-controlled Phase III clinical studies, each providing convincing evidence of safety and effectiveness. *See Warner-Lambert Co. v. Heckler*, 787 F.2d 147 (3d Cir. 1986); Final Decision on Benlylin, 44 Fed. Reg. 51,512, 51,518 (Aug. 31, 1979). However, the Food and Drug Administration Modernization Act of 1997, revised the standard to provide that "[i]f the Secretary [of Health and Human Services] determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence . . ." 21 U.S.C. § 355(d) (2012).

¹³⁰ Generally, the NDA should contain reports on the following: 1) chemistry, manufacturing, and control; 2) nonclinical pharmacology and toxicology; 3) human pharmacokinetics and bioavailability; and 4) clinical efficacy and safety data. *See* 21 C.F.R. § 314.50 (2012).

¹³¹ *See* IOM, *THE FUTURE OF DRUG SAFETY*, *supra* note 111, at 39.

¹³² CDER may refuse to file a NDA for a variety of reasons, including the failure to conclude evidence of effectiveness compatible with the FDCA and regulations. *See* 21 C.F.R. § 314.101(d)(3) (2012).

¹³³ 21 U.S.C. § 355(c) (2012).

¹³⁴ The FDA takes the position that each time a drug sponsor submits new information to the FDA, the clock restarts. *See Merrill*, *supra* note 123, at 1766 (noting that if drug sponsors pushed for a decision within 180 days, the answer may be "no," and appealing the decision would likely be futile).

¹³⁵ For many of the NDAs, the FDA may convene an advisory committee as a source of independent advice from experts outside of the FDA. The FDA has seventeen advisory committees. Typically, advisory committees will meet with the drug manufacturer and FDA representatives before voting on the drug. The FDA is not bound by the vote of the advisor committee. *See* IOM, *THE FUTURE OF DRUG SAFETY*, *supra* note 111, at 45–46.

¹³⁶ 21 C.F.R. § 314.50 (2012).

¹³⁷ *Id.* § 312.84.

¹³⁸ *See* SUSAN THAUL, CONG. RESEARCH SERV., R41983, HOW FDA APPROVES DRUGS AND REGULATES THEIR SAFETY AND EFFECTIVENESS (2012), available at <http://www.fas.org/sgp/crs/misc/R41983.pdf>.

The review team is typically comprised of reviewers from the Office of New Drugs (OND) and CDER with various medical and scientific specialties. The primary reviewer is responsible for preparing and signing the written review of the NDA. The primary reviewer summarizes and analyzes the clinical data in the NDA¹³⁹ and provides the reviewer's assessments and conclusions regarding the effectiveness and safety data.¹⁴⁰ The other scientific reviewers will each write and design "discipline reviews" that evaluates the NDA from the area of their expertise and the primary reviewer summarizes those reviews.¹⁴¹

FDA reviewers base their assessments not simply on the data submitted by drug manufacturers¹⁴² but also compile and reanalyze the data submitted.¹⁴³ In contrast, the FDA's European counterparts typically rely almost exclusively on data submitted by drug manufacturers. During the review process, sometimes the FDA will ask drug manufacturers for additional information and drug manufacturers will amend an NDA. If the FDA is convinced that the manufacturer has produced "substantial evidence" of drug safety and effectiveness, then the drug is approved.¹⁴⁴ If the manufacturer has not met its burden, then the FDA has two options: not approve¹⁴⁵ or deem the drug approvable.¹⁴⁶ The FDA's decision is conveyed to the drug sponsor in a complete response letter.¹⁴⁷

¹³⁹ Drug sponsors must submit to the FDA the "full reports" of all studies conducted to ascertain the safety and effectiveness of the drug. *See* 21 U.S.C. § 355(b)(1)(A) (2012) (requiring submission of "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use").

¹⁴⁰ FDA regulations provide that studies submitted to the FDA should provide a clear statement of purpose, permit a valid comparison of the experimental group with a control group; employ suitable methods to assign study and control groups and otherwise to minimize bias; use clear, reliable methods to define and assess responses of research participants; and employ appropriate methods to analyze study results. *See* 21 C.F.R. § 314.126 (2012).

¹⁴¹ *See* IOM, *THE FUTURE OF DRUG SAFETY*, *supra* note 111, at 43.

¹⁴² Since the FDA relies on self-reported data, it promulgated specific regulations to ensure the integrity of the process in which the scientific data is collected. The FDA requires drug sponsors to designate "monitors" to oversee the conduct of any clinical trial that it sponsors. Monitors interact with researchers to ensure that the trials comply with applicable standards of scientific integrity, conform to protocol, and protect human research participants. *See* 21 C.F.R. §§ 312.50-.70 (2012).

¹⁴³ *See* IOM, *THE FUTURE OF DRUG SAFETY*, *supra* note 111, at 44.

¹⁴⁴ An approval letter notifies the drug manufacturer that the drug has been approved and details labeling and other postmarketing requirements. Sometimes if the FDA has lingering concerns about a drug, the FDA will elect to condition approval upon the manufacturer agreeing to conduct post-market clinical trials (often referred to as Phase IV studies). *See* 21 C.F.R. § 312.85 (2012).

¹⁴⁵ A letter denying approval explains the deficiencies in the application, including each applicable ground for denial under sections 360e(d)(2)(A)-(E) of the FDCA. 21 U.S.C. §§ 360e(d)(2)(A)-(E) (2012).

¹⁴⁶ The approval letter means that the FDA deems the drug approved if certain specific additional steps are taken. *See* IOM, *THE FUTURE OF DRUG SAFETY*, *supra* note 111, at 51.

¹⁴⁷ *See* 21 C.F.R. § 314.110(a) (2012).

III. THE FDA'S PATH TO REGULATORY FAILURE

The current merit-based drug approval paradigm is clearly broken. Since the 1962 Amendments, the FDA in essence has had unchallengeable authority to demand any number of different kinds of studies to prove approval worthiness and virtually unreviewable discretion to interpret the results. Before the 1962 Amendments, the time lag from discovery of a compound until its approval by the FDA took about two and a half years.¹⁴⁸ Presently, the time-lag from discovery until approval by the FDA is about ten to thirteen years.¹⁴⁹

Because of the time and resources necessary to bring a drug to the market, drug development costs have mushroomed. The cost to develop a new drug in the 1960s was about \$92 million,¹⁵⁰ compared to a current average of \$1.3 billion.¹⁵¹ Further, the increasing cost and regulatory hurdles associated with developing drugs has curtailed innovation.¹⁵² Drug approvals plummeted from a high of fifty-three in 1996 to a nearly record low of twenty-one in 2010 before edging higher in 2012.¹⁵³

A. *Approving Unsafe Drugs*

The FDA's failures have been widely publicized. Between 2000 and 2011, twenty-six FDA approved drugs were withdrawn because of safety concerns.¹⁵⁴ Few people are unfamiliar with such high profile failures

¹⁴⁸ See Roberts & Bodenheimer, *supra* note 106, at 586.

¹⁴⁹ See Rebecca Henderson & Cate Reavis, *Eli Lilly: Recreating Drug Discovery for the 21st Century* 16 (MIT Sloan Sch. of Mgmt., Paper No. 07-043, 2008), available at <https://mitsloan.mit.edu/LearningEdge/CaseDocs/07-043-Recreating-Drug-Discovery.pdf>.

¹⁵⁰ See Morgan, *supra* note 118, at 10.

¹⁵¹ See Matthew Herper, *The Truly Staggering Cost of Inventing New Drugs*, FORBES (Feb. 10, 2012, 7:41 AM), <http://www.forbes.com/sites/matthewherper/2012/02/10/the-truly-staggering-cost-of-inventing-new-drugs> ("Eli Lilly posted . . . that the average cost of bringing a new drug to market is \$1.3 billion, a price that would buy 371 Super Bowl ads, 16 million official NFL footballs, two pro football stadiums, pay of almost all NFL football players, and every seat in every NFL stadium for six weeks . . .").

¹⁵² See DAVID GRATZER, *THE CURE: HOW CAPITALISM CAN SAVE AMERICAN HEALTH CARE* 152 (2006) ("The bureaucratic hurdles, in other words, have been set too high. FDA caution is undermining our ability to make new drugs and save lives."); Roberts & Bodenheimer, *supra* note 106, at 602 (noting that the 1962 Amendments have had a negative impact on innovation, including reduced research of new chemical entities and earlier introduction of American drugs in foreign countries).

¹⁵³ See Ben Hirschler & Caroline Humer, *FDA New Drug Approvals Hit 16-year High in 2012*, REUTERS (Dec. 31, 2012, 4:55 PM), <http://www.reuters.com/article/2012/12/31/us-pharmaceuticals-fda-approvals-idUSBRE8BU0EK20121231> (noting that although thirty-nine new drugs were approved, many of the approvals were for niche products to treat rare conditions).

¹⁵⁴ The drugs withdrawn include Bextra, which ended in a class action settlement of \$894 million covering 7,000 plaintiffs, of whom 10% were relatives of people who died as a result of taking Bextra. See Linda A. Johnson, *Pfizer Reaches Massive Settlement in Celebrex, Bextra*

like Vioxx¹⁵⁵ and Avandia.¹⁵⁶ Although Vioxx and Avandia received media attention because of the millions of Americans who were

Lawsuits, HUFFINGTON POST (Oct. 17, 2008, 9:05 PM), http://www.huffingtonpost.com/2008/10/17/pfizer-reaches-massive-se_n_135518.html; see also *infra* notes 155 (noting that Vioxx caused the death of nearly 3,500 and injured thousands more) & 156 (noting that Avandia caused over 80,000 heart attacks).

¹⁵⁵ Merck was granted approval by the FDA to market rofecoxib under the trade name Vioxx for the management of acute pain in adults and for relief of the signs and symptoms of osteoarthritis on May 20, 1999. The drug was withdrawn from the market on September 30, 2004 because the drug was linked to an increased risk of heart attacks and strokes. See Walter T. Champion, *The Vioxx Litigation Paradigm: The Search for Smoking Guns*, 31 T. MARSHALL L. REV. 157 (2006). By the time Vioxx was withdrawn, yearly sales exceeded \$1 billion per year. Ultimately, Merck settled claims for roughly \$4.58 billion. See, e.g., David Voreacos & Allen Johnson, *Merck Paid 3,468 Death Claims to Resolve Vioxx Suits*, BLOOMBERG (July 27, 2010, 5:27 PM), <http://www.bloomberg.com/news/2010-07-27/merck-paid-3-468-death-claims-to-resolve-vioxx-suits.html> (noting that 2,878 Vioxx users died of heart attacks and 590 died of strokes). Merck also agreed to pay \$58 million as part of a multistate settlement of accusations that its ads for Vioxx deceptively played down the health risks. In addition to the monetary sum, the agreement called for Merck to submit all new television commercials for its drugs to the FDA for seven years and to abide by any changes the agency recommends. For a ten-year period, Merck must also comply with any FDA recommendations to delay television ads for newly approved pain medications. See Associated Press, *Merck Settles with States on Vioxx Ads*, N.Y. TIMES, May 21, 2008, at C3. Unsurprisingly, both the FDA and Merck were widely criticized. See, e.g., Brooke A. Masters & Marc Kaufman, *Painful Withdrawal for Makers of Vioxx: Pulling of Arthritis Drug Raises Questions on Marketing, Safety Risks*, WASH. POST, Oct. 18, 2004, at A1 (noting that even when Merck was aware of safety issues, it released “a \$195 million ad campaign, featuring testimonials from former skater Dorothy Hamill and music by the Rascals to appeal to aging baby boomers”); Eric J. Topol, *Failing the Public Health—Rofecoxib, Merck, and the FDA*, 351 NEW ENG. J. MED. 1707 (2004), available at <http://www.nejm.org/doi/full/10.1056/NEJMp048286> (strongly criticizing the FDA for not stopping the marketing and distribution of Vioxx when the research initially indicated that the drug was not safe).

¹⁵⁶ Avandia was manufactured by GlaxoSmithKline (GSK). It was approved by the FDA in 1999 and labeled for the treatment of type-2 diabetes. Like Vioxx, Avandia became a blockbuster drug, generating over \$3 billion in sales annually. Unfortunately, Avandia significantly increased the risk of having a heart attack for diabetes patients. It is estimated that Avandia caused about 83,000 heart attacks. Even more troubling, GSK “attempted to intimidate independent physicians, focused on strategies to minimize or misrepresent findings that Avandia may increase cardiovascular risk, and sought ways to downplay findings that a competing drug might reduce cardiovascular risk.” STAFF OF S. COMM. ON FIN., 111TH CONG., REP. ON GLAXOSMITHKLINE AND THE DIABETES DRUG AVANDIA 1 (Comm. Print 2010) (Max Baucus & Chuck Grassley), available at <http://www.finance.senate.gov/library/prints>. Ultimately, GSK entered into a \$3 billion settlement, the largest health care fraud settlement in United States history, for unlawful promotion of drugs including Avandia, failure to report certain safety data, and other illegal acts. Press Release, Dep’t of Justice, *GlaxoSmithKline to Plead Guilty and Pay \$3 Billion to Resolve Fraud Allegations and Failure to Report Safety Data* (July 2, 2012), available at <http://www.justice.gov/opa/pr/2012/July/12-civ-842.html>. In addition to the settlement with the government, GSK also paid at least \$700 million to settle lawsuits with over 15,000 patients who claimed to have suffered heart attacks or strokes. See Jef Feeley, *Glaxo Settles 20,000 Lawsuits over Avandia, Lawyer Says*, BLOOMBERG (Feb. 1, 2012, 6:01 PM), <http://www.bloomberg.com/news/2012-02-01/glaxosmithkline-agrees-to-settle-20-000-more-avandia-cases-lawyer-says.html>. In spite of the fines and settlements, GSK still made a profit. Total sales for Avandia based on IMS data is estimated to be over \$10.4 billion. See Alexandra Sifferlin, *Breaking Down GlaxoSmithKline’s Billion-Dollar Wrongdoing*, TIME MAG. (July 5, 2012), <http://healthland.time.com/2012/07/05/breaking-down-glaxosmithklines-billion-dollar-wrongdoing>.

prescribed the drugs, there are many other withdrawals that received far less media attention. Since 2009, Raptiva,¹⁵⁷ Meridia,¹⁵⁸ Mylotarg,¹⁵⁹ Darvon,¹⁶⁰ Avandia,¹⁶¹ and Xigris¹⁶² have been withdrawn.

Short of withdrawing a particular drug from the market, the FDA regularly revises warnings associated with many drugs after approval. This occurs when new studies find that the drug carries serious risks that were not known when approved.¹⁶³ For example, between 2004 and 2006, the FDA issued seventy-seven new black box warnings.¹⁶⁴ Black

¹⁵⁷ Press Release, U.S. Food & Drug Admin., FDA Statement on the Voluntary Withdrawal of Raptiva from the U.S. Market (Apr. 8, 2009), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm149561.htm> (noting that Genentech is withdrawing Raptiva “because of a potential risk to patients of developing progressive multifocal leukoencephalopathy (PML), a rare, serious, progressive neurologic disease caused by a virus that affects the central nervous system”).

¹⁵⁸ See Andrew Pollack, *Abbott Labs Withdraws Meridia, its Diet Drug, from the Market*, N.Y. TIMES, Oct. 8, 2010, at B3 (noting that Dr. John Jenkins, Director of the Office of New Drugs said in a statement that “Meridia’s continued availability is not justified when you compare the very modest weight loss that people achieve on this drug to their risk of heart attack or stroke” (internal quotation marks omitted)).

¹⁵⁹ Press Release, U.S. Food & Drug Admin., FDA: Pfizer Voluntarily Withdraws Cancer Treatment Mylotarg from U.S. Market (June 21, 2010), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm216448.htm> (noting that the drug was being withdrawn “after results from a recent clinical trial raised new concerns about the product’s safety and the drug failed to demonstrate clinical benefit to patients enrolled in trials”).

¹⁶⁰ See Andrew Zajac, *Painkillers Darvon, Darvocet Being Withdrawn; The Widely Prescribed Medications are Linked to Serious Heart Rhythm Abnormalities*, L.A. TIMES, Nov. 20, 2010, at A20 (reporting that the painkilling drug was withdrawn because the active ingredient was linked to “serious and sometimes fatal heart rhythm abnormalities”).

¹⁶¹ See *supra* note 156.

¹⁶² See Press Release, Eli Lilly & Co., Lilly Announces Withdrawal of Xigris Following Recent Clinical Trial Results (Oct. 25, 2011), available at <http://newsroom.lilly.com/releasedetail.cfm?releaseid=617602> (“While there were no new safety findings, the [PROWESS-SHOCK] study, failed to demonstrate that Xigris improved patient survival and thus calls into question the benefit-risk profile of Xigris and its continued use.” (quoting Timothy Garnett, M.D., Lilly’s Senior Vice President and Chief Medical Officer)).

¹⁶³ For instance a whole class of antidepressants known as Selective Serotonin Reuptake Inhibitors (SSRIs) have received negative publicity about increased health risks. These drugs are widely known and prescribed, in part, because of robust direct-to-consumer advertising campaigns. See, e.g., Benedict Carey & Roni Caryn Rabin, *Study Finds Drug Risks with Newer Antipsychotics*, N.Y. TIMES, Jan. 15, 2009, at A24 (reporting on a Vanderbilt study that found that patients who took the new antipsychotic drugs doubled their chance of having a heart attack); Duff Wilson, *Heart Warning Added to Label on Popular Antipsychotic Drug*, N.Y. TIMES, July 19, 2011, at B7 (reporting that Serequel had sales of \$3.7 billion in 2010, and the FDA was revising the labeling to include a warning of increased heart attack risks when used in combination with other drugs); see also Gina Kolata, *When Drugs Cause Problems They Are Supposed to Prevent*, N.Y. TIMES, Oct. 17, 2010, at A18 (noting that bisphosphonates, which are widely used to prevent fractures that are common in people with osteoporosis, will now have a revised label indicating that use can lead to rare fractures of the thigh bone and can cause rare degeneration of the jawbone).

¹⁶⁴ See Daniel M. Cook, Rama K. Gurugubelli, & Lisa A. Bero, *Risk Management Policy and Black-Box Warnings: A Qualitative Analysis of US FDA Proceedings*, 32 DRUG SAFETY 1057, 1060 (2009).

box warnings are given when the data suggests that there is a possibility of the drug causing serious or life-threatening risks.¹⁶⁵

The fault lies not with the FDA reviewers. Instead, the blame lies with a faulty merit-based paradigm. Estimates suggest that half of all new drugs approved have at least one serious adverse effect that is unknown at the time of drug approval.¹⁶⁶ Only “[o]ne-third of all drugs act as expected when prescribed to patients.”¹⁶⁷ Further, medicine as a whole remains more of an art than a science, with physicians acknowledging that only 20–25% of current medical practice has been proven effective.¹⁶⁸

The FDA’s merit-based regulatory paradigm is based on a myth. It is impossible to fully understand the safety profile of a drug before it is widely prescribed. This is true for a number of reasons. First, the number of participants exposed to the drug in clinical trials is relatively small compared to the number of people who will be prescribed the drug. Thus, it is nearly impossible to identify rare but serious adverse events in the context of clinical trials.¹⁶⁹

Second, when a drug is widely prescribed, the patients who are prescribed the drugs will often also take additional other drugs for other medical conditions. However, clinical testing does not test compatibility with other drugs. For example, Seldane, a blockbuster drug,¹⁷⁰ was approved in 1985 and withdrawn from the market in 1998.¹⁷¹ Although safe when used alone, post-approval it became clear that when

¹⁶⁵ See *A Guide to Drug Safety Terms at FDA*, FDA CONSUMER HEALTH INFO., U.S. FOOD & DRUG ADMIN. (Nov. 2012), at 1, available at <http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/ucm107976.pdf>.

¹⁶⁶ See Thomas N. Tiedt, *The Drug Safety System Conundrum*, 62 FOOD & DRUG L.J. 548, 553 (“Fifty-one percent of all approved drugs elicit at least one serious type of adverse reaction that was not observed during premarketing clinical trials . . .”).

¹⁶⁷ Jeffrey P. Braff et al., *Patient-Tailored Medicine, Part One: The Impact of Race and Genetics on Medicine*, 2 J. HEALTH & LIFE SCI. L. 1, 16 (2008), available at http://www.healthlawyers.org/Events/Programs/Materials/Documents/AM12/papers/Q_holmes_matyas_patient_taylored_medicine_p1.pdf.

¹⁶⁸ See John Carey, *Medical Guesswork*, BLOOMBERG BUSINESSWEEK (May 28, 2006), <http://www.businessweek.com/stories/2006-05-28/medical-guesswork> (“We don’t have the evidence [that treatments work], and we are not investing very much in getting the evidence.” (alteration in original) (quoting Dr. Stephen C. Schoenbaum, executive vice-president of the Commonwealth Fund and former president of Harvard Pilgrim Health Care, Inc.) (internal quotation marks omitted)).

¹⁶⁹ See IOM, *THE FUTURE OF DRUG SAFETY*, *supra* note 111, at 37 (noting that a serious adverse event “that occurs in less than one in 1,000 patients cannot be reliably detected except in the largest premarket trials”).

¹⁷⁰ Seldane was the first treatment for allergies that did not cause drowsiness. In the year following its approval, it had \$400 million in sales. See Marlene Cimons, *FDA Says Seldane Should Be Withdrawn*, L.A. TIMES (Jan. 14, 1997), http://articles.latimes.com/1997-01-14/news/mn-18552_1_seldane-fda-withdrawn; Michael A. Friedman et al., *The Safety of Newly Approved Medicines: Do Recent Market Removals Mean There is a Problem?*, 281 JAMA 1728, 1729 (1999).

¹⁷¹ See Friedman et al., *supra* note 170, at 1728–29, 1729 n.20.

prescribed with certain other drugs, the interaction caused fatal cardiac arrhythmias.¹⁷²

Third, clinical trials also draw from limited patient populations. For example, clinical trials often have trouble recruiting participants from diverse ethnic backgrounds.¹⁷³ This is particularly troubling because studies that are racially inclusive have shown race-based differences in adverse reactions to some medications.¹⁷⁴ As an example, the clinical trials for BiDil were comprised of a diverse group of patients. The clinical testing revealed that BiDil was not effective for treating heart failure in white patients but was effective for black patients. As a result, BiDil became the first drug approved for a particular racial group.¹⁷⁵ In addition to minorities, the elderly, pregnant women, and children are often excluded from clinical trials.¹⁷⁶

Lastly, as a consequence of their inherent design, clinical trials are incapable of detecting long-term risk. Phase III clinical trials typically last less than four years, and during that time only a few hundred patients typically receive the new drug for more than three to six months.¹⁷⁷ The Institute of Medicine has noted in one of its recent studies that “only the most profound and overt risks and side effects that occur immediately after taking a drug can be detected . . . Risks that are

¹⁷² See *id.* at 1731. Hoechst, the pharmaceutical manufacturer, developed a new product that provided the same therapeutic effects without the side effects when prescribed in combination with other drugs and, at the FDA’s request, withdrew Seldane. See *id.* at 1729.

¹⁷³ Patrick Y. Lee et al., *Representation of Elderly Persons and Women in Published Randomized Trials of Acute Coronary Syndromes*, 286 JAMA 708 (2001) (finding that the elderly and women are underrepresented in clinical trials); Roxanne Nelson, *Minorities Still a Minority in Clinical Trials*, MEDSCAPE TODAY (Feb. 10, 2009), <http://www.medscape.com/viewarticle/588096> (“[R]acial and ethnic minorities continue to be underrepresented in clinical trials.”).

¹⁷⁴ For instance, post-marketing studies of Crestor, a cholesterol-lowering drug commonly referred to as a “statin,” found that Asian-Americans taking Crestor had a two-fold elevation of the drug in their blood as compared to Caucasians, increasing their risk for adverse reactions. Thus, the FDA revised the labeling to include a recommendation that Asians start Crestor at a five-milligram dosage. See *FDA Public Health Advisory for Crestor (rosuvastatin)*, U.S. FOOD & DRUG ADMIN., (March 2, 2005), <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/PublicHealthAdvisories/ucm051756.htm>.

¹⁷⁵ See Robert Temple & Norman L. Stockbridge, *BiDil for Heart Failure in Black Patients: The U.S. Food and Drug Administration Perspective*, 146 ANNALS INTERNAL MED. 52 (2007), available at <http://annals.org/article.aspx?articleid=477597> (noting that the clinical trials showed strong evidence that the drug was extremely effective in black patients but that the effects were much smaller or not present at all in white patients). The approval of BiDil for a specific racial group was a first for the FDA and generated intense debate. See, e.g., Gregory Michael Dorr & David S. Jones, *Introduction: Facts and Fictions: BiDil and the Resurgence of Racial Medicine*, 36 J.L. MED. & ETHICS 443 (2008); Sharona Hoffman, “Racially-Tailored” *Medicine Unraveled*, 55 AM. U. L. REV. 395, 410 (2005).

¹⁷⁶ See IOM, THE FUTURE OF DRUG SAFETY, *supra* note 111, at 38.

¹⁷⁷ See IOM, PREVENTING MEDICATION ERRORS, *supra* note 103, at 55–56.

medically important but delayed . . . may not be revealed prior to marketing.”¹⁷⁸

Because clinical trial populations are limited in size and scope, the true safety profile of a drug cannot be ascertained based upon pre-market clinical trials.¹⁷⁹ For this reason, the FDA is doomed to continue failing in its role as merit-regulator. The current paradigm insists on evaluating merit before the merit can be ascertained.

B. *Approving Ineffective Drugs*

The merit-based regulatory paradigm not only fails to prevent unsafe drugs from entering the market place, but it also allows ineffective drugs into the marketplace. For example, Mibefradil¹⁸⁰ was withdrawn after approval because it was discovered that it posed serious risks without being more effective than existing treatments. Mibefradil was absolutely safe when taken alone. However, it “reduced the activity of several isoenzymes” in the liver, which are vital to eliminating “a variety of drugs from the body.”¹⁸¹ This interaction was noted in clinical trials and included in the initial labeling. Nonetheless, a number of patients were still prescribed Mibefradil in combination with other drugs. In response, the FDA amended the label and strengthened the warning.¹⁸² But, when post-approval studies demonstrated that Mibefradil was not more effective than existing treatments, the FDA took the position that the benefits of the drug did not outweigh the risks—since it was known to cause interactions with twenty-six widely prescribed medications—and requested removal.¹⁸³

Mibefradil is not an isolated example.¹⁸⁴ In many cases, new drugs are approved and assumed to be more effective with fewer side effects

¹⁷⁸ See *id.* at 56.

¹⁷⁹ See GRATZER, *supra* note 152, at 157 (“[D]espite the extraordinary caution of the FDA, it’s difficult to tell exactly how a drug affects people until it hits pharmacies. Bromfenac is a case in point. No problems had been discovered by the original clinical trials, involving 2,500 people. The analgesic was withdrawn after causing four deaths and necessitating eight liver transplants—but the medication was taken by 2.5 million people.” (footnote omitted)).

¹⁸⁰ Mibefradil is a calcium-channel blocker and had been approved for the treatment of patients with hypertension or chronic stable angina. See Barbara Apgar, *Mibefradil: A T-Type Calcium Channel Blocker*, 57 AM. FAM. PHYSICIAN 1946 (1998); Roy G. Beran, *The Ethics of Post-Marketing Surveillance of Therapeutic Agents*, 20 MED. & L. 587, 590 (2001).

¹⁸¹ Friedman et al., *supra* note 170, at 1729.

¹⁸² See *id.*

¹⁸³ See *id.*

¹⁸⁴ There is little incentive for pharmaceutical companies to conduct comparative studies because newer often does not equate with better. For example, a post-market comparative trial of newer hypertension agents—angiotensin-converting enzyme (ACE) inhibitors—against older diuretic drugs, for example, found the older drugs to be more effective at reducing blood pressure. See Lawrence J. Appel, *The Verdict from ALLHAT—Thiazide Diuretics Are the*

than older treatments, only to have that notion proven incorrect by post-marketing studies.¹⁸⁵ Again, fault lies not with the reviewers but with the regulatory paradigm. The pre-market clinical trials provide at best an incomplete basis for assessing safety. Drug sponsors are not required to test their drugs against current treatments. They are only required to use a placebo.¹⁸⁶ Consequently, FDA reviewers do not have adequate information to assess the merit of the drug. This leads to approval of drugs that are unsafe and ineffective and delay or lack of approval of drugs that are safe and effective.¹⁸⁷

IV. A PROPOSAL FOR REGULATORY REFORM: SHARED MISSION, SHARED PATH

Reform is needed, as the current regulatory paradigm is broken. The merit-based approval structure is ineffective, paternalistic, and costly. Dangerous drugs are approved, causing serious harm and even death.¹⁸⁸ Congressional hearings are held to investigate these failures, giving FDA reviewers greater incentive to worry about the next Vioxx¹⁸⁹

Preferred Initial Therapy for Hypertension, reprinted in 288 JAMA 3039 (2002) (finding that the older, less expensive therapy was also the more effective).

¹⁸⁵ New atypical anti-psychotic drugs like Risperdal, Zyprexa, Seroquel, and Abilify were approved beginning in the 1990s with the promise of being more effective than older antipsychotics. However, post-marketing clinical trials failed to show that these atypical drugs were more effective or better tolerated than the older antipsychotics. The trials also showed serious side effects associated with the new drugs, including increased blood sugar and elevated cholesterol levels. See Richard A. Friedman, *A Call for Caution on Antipsychotic Drugs*, N.Y. TIMES, Sept. 24, 2012, at D6. In addition, the use of statins for prevention of heart attacks has been questioned after nearly 24 million prescriptions have been filled. See Melissa Healy, *Rethinking Statins; Use of the Drugs has Soared. But Some Question if All Benefit*, L.A. TIMES, Aug. 9, 2010, at E1 (reporting that some doctors are questioning whether statins are effective at reducing the risk of a first heart attack in people, also called “primary prevention”).

¹⁸⁶ See 21 C.F.R. § 314.126(b)(2)(i) (2012) (providing that the study design may use a “[p]lacebo concurrent control” that compares “[t]he test drug . . . with an inactive preparation designed to resemble the test drug”).

¹⁸⁷ *Contra* 21 U.S.C. § 393 (2012).

¹⁸⁸ See, e.g., Michael J. Malinowski, *Doctors, Patients, and Pills—A System Popping Under Too Much Physician Discretion? A Law-Policy Prescription to Make Drug Approval More Meaningful in the Delivery of Health Care*, 33 CARDOZO L. REV. 1085, 1110–11 (2012) (“The public has lost confidence in the FDA, and for good reason. The FDA withdrew ten drugs for safety concerns between 2000 and March 2006 . . .” (footnote omitted)).

¹⁸⁹ See HENRY G. GRABOWSKI, *DRUG REGULATION AND INNOVATION: EMPIRICAL EVIDENCE AND POLICY OPTIONS* 75–76 (1976). For example, former FDA Commissioner, Alexander Schmidt, in a speech, said:

[f]or example, in all of [the] FDA’s history, I am unable to find a single instance where a Congressional committee investigated the *failure* of [the] FDA to approve a new drug. But, the times when hearings have been held to criticize our approval of new drugs have been so frequent that we aren’t able to count them . . . The message of FDA staff could not be clearer. Whenever a controversy over a new drug is

than about exercising undue deliberations or vigilance in delaying or denying new drug approvals.¹⁹⁰

At the same time, the costs associated with developing a new drug have eclipsed \$1 billion dollars,¹⁹¹ and the time-lag from discovery of a new drug until approval is over a decade.¹⁹² Delayed access to new drugs has not only increased capital costs, but human costs as well.¹⁹³

Further, in spite of increased statutory mandates from Congress, the FDA's budget is stagnant, and critical departments are understaffed and underfunded.¹⁹⁴ Yet, NDA review is insulated from funding cuts and taking up an increased percentage of the FDA's budget. Nearly 40% of the FDA's budget is allocated to merit review.¹⁹⁵ Over 1,000 employees are assigned to reviewing NDAs for an average of 100 new drug applications, while a minuscule 100 employees are assigned to monitoring adverse events for the four billion prescriptions filled in the United States each year.¹⁹⁶

resolved by its approval, the Agency and the individuals involved likely will be investigated. Whenever such a drug is disapproved, no inquiry will be made.

Id. at 76 (omission in original) (quoting Alexander Schmidt, Comm'r, Food & Drug Admin., *The FDA Today: Critics, Congress and Consumerism*, Speech before the National Press Club (Oct. 29, 1974)).

¹⁹⁰ Nonetheless, there have been a few times when public pressure has been applied to the FDA for being too cautious in approving drugs. See generally Kenneth I. Kaitin & Jeffrey S. Brown, *A Drug Lag Update*, 29 *DRUG INFO. J.* 361 (1995).

¹⁹¹ See Herper, *supra* note 151.

¹⁹² See Henderson & Reavis, *supra* note 149 (noting that average time lag from discovery of a new drug until approval is between ten and thirteen years).

¹⁹³ For example, researchers have calculated the cost of preventable deaths from drugs approved and withdrawn since the passage of the Prescription Drug User Fee Act of 1992 (PDUFA), see *infra* note 195, at 56,000 life-years saved versus 180,000 to 310,000 life-years saved through the more rapid introduction of drugs under the Act. See Tomas Philipson et al., *How Safe is Too Safe?: Public Safety Versus Innovation at the FDA*, 2 *MILKEN INST. REV.* 38, 38, 45 (2006), available at http://www.milkeninstitute.org/publications/review/2006_6/38_45mr30.pdf.

¹⁹⁴ See Peter Barton Hutt, *The State of Science at the Food and Drug Administration*, 60 *ADMIN. L. REV.* 431, 455 (2008) (discussing the lack of funding for the FDA and a "steady erosion in its human capital").

¹⁹⁵ See *id.* at 454. The Prescription Drug User Fee Act of 1992, Pub. L. No. 102-51, 106 Stat. 4491, instituted user fees. Pharmaceutical companies thus pay fees for submitting NDAs and other filings. In exchange for the fees, Congress is required to maintain its normal appropriations for review functions, indexed for inflation, and the FDA must achieve performance goals. PDUFA has been reauthorized every five years since 1992. The latest reauthorization was signed into law on July 9, 2012 as part of the FDA Safety and Innovation Act. FDA's current performance goal is to review and act upon 90% of priority review applications within six months, and 90% of standard review applications within ten months. Renu Lal, *PDUFA V*, *FDA/CDER SMALL BUS. CHRON.* (FDA/CDER Small Bus. Assistance, Silver Spring, Md.), Oct. 12, 2012, at 1, available at <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM323487.pdf>.

¹⁹⁶ See Parasidis, *supra* note 8, at 930 n.2 (citing Vishal Jain & C. S. Pitchumoni, *Gastrointestinal Side Effects of Prescription Medications in the Older Adult*, 43 *J. CLINICAL GASTROENTEROLOGY* 103, 103 (2009)) (noting that there are over four billion prescriptions filled in the United States each year).

With the budgetary woos in Washington, it is unrealistic to believe that the FDA will benefit from a huge increase in appropriations in the near future. Consequently, this proposal does not require increased funding for the FDA. This proposal calls for a budgetary neutral shift in the FDA's focus from merit-regulation to disclosure regulation. This proposal is structured around three key elements: (1) repeal of the 1962 amendments; (2) increased access to the clinical trial database; and (3) expansion of adverse reporting duties.

A. *Elimination of Merit-Regulation*

Clinical trials offer only a small window into the risk profile of a drug for a limited patient population. As previously discussed, pre-approval testing is usually incapable of detecting adverse events occurring rarely,¹⁹⁷ having long latency periods,¹⁹⁸ or affecting specific subpopulations not adequately represented in trials.¹⁹⁹ Thus, the FDA is protecting the public's health by assessing merit based on data that is extremely limited and largely unreliable. Consequently, the FDA is failing at its mission.

As a remedy, my proposal calls for a shift to a drug approval paradigm that is conditioned upon drug sponsors submitting evidence to the FDA, extrapolated from clinical trials, that the drug is safe and effective for each proposed indication.²⁰⁰ Similar to the regime prior to 1962, the FDA would have sixty days to reject the application if the application is incomplete or if the clinical data suggests that the drug poses an imminent and grave risk to public health.²⁰¹ After sixty days, unless the FDA intervenes, the drug would automatically be approved for the indications requested by the sponsor, and the drug sponsor would be free to market the drug.

¹⁹⁷ See *supra* note 169.

¹⁹⁸ See IOM, PREVENTING MEDICATION ERRORS, *supra* note 103, at 55.

¹⁹⁹ See IOM, THE FUTURE OF DRUG SAFETY, *supra* note 111, at 38 (noting that pediatric patients, the elderly, and pregnant women are usually excluded from clinical trials).

²⁰⁰ Under this proposal, the FDA would retain its authority to approve INDs. Thus, a drug sponsor would need FDA approval prior to testing a drug compound in humans. However, once an IND is approved, drug sponsors would be free to advance through the different clinical trial stages without needing FDA approval. The clinical trial data would still need to be submitted with the NDA, including at least one adequately controlled stage III clinical trial, in order to be approved.

²⁰¹ This standard would mirror the Restatement (Third) of Torts: Products Liability. See RESTATEMENT (THIRD) OF TORTS: PROD. LIAB. § 6(c) (1998) ("A prescription drug or medical device is not reasonably safe due to defective design if the foreseeable risks of harm posed by the drug or medical device are sufficiently great in relation to its foreseeable therapeutic benefits that reasonable health-care providers, knowing of such foreseeable risks and therapeutic benefits, would not prescribe the drug or medical device for any class of patients.").

In addition, drug sponsors would be obligated to supplement their initial NDA applications with results from a completed post-market Phase IV clinical trial within five years from the date of approval. If the drug sponsor fails to conduct and complete the Phase VI trial, the drug's approval would be automatically revoked, making continued marketing of the drug a violation of the FDCA.

The over-arching goal of this proposal is to eliminate merit-regulation. This proposal has a number of advantages over the current merit-based paradigm. First, it relieves the manufacturers of the burden of seeking FDA approval to advance through each phase of the clinical trial process. Under this proposal, drug manufactures, in conjunction with the IRB, will have unilateral decision-making authority to advance a drug through the clinical trial process. The FDA does not need to maintain an active oversight role of the clinical trial process because the IRBs are legally required to ensure that federal guidelines are followed.²⁰² Additionally, manufactures will still need to acquire IRB approval to proceed with each clinical trial phase.

Second, this proposal will reduce costs. From the manufacturer's perspective, costs will decrease because the length of the clinical trial process will decrease. Protracted negotiations with the FDA about repeating Phase II clinical trials will be eliminated. Further, at the FDA, the personnel needed and costs associated with NDA review will be sharply curtailed. By eliminating the FDA's role as merit-regulator, the number of employees assigned to culling and re-analyzing the 100,000 pages of data submitted in the NDA will be drastically reduced; as a result, more employees can be allocated to post-market surveillance and other areas of enforcement that are understaffed.

Third, this proposal should settle the preemption debate. Since the FDA would no longer be engaging in merit-regulation, the FDA could not credibly argue that state law failure-to-warn claims are preempted.²⁰³ State tort liability is necessary to deter corporate misbehavior and offers compensation to those injured by unknown adverse side effects.

Finally, this proposal should provide the public with quicker access to needed drugs without compromising safety. Under this proposal, the FDA retains the authority to prevent an unreasonably risky drug from being marketed. If based on the data submitted, the FDA concludes that

²⁰² The IRB reviews each research protocol to determine whether subject selection is equitable, whether the risk is proportional to the benefits, and whether the confidentiality of any data that are collected will be adequately protected. See 45 C.F.R. § 46.111 (2012).

²⁰³ See David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-To-Warn Claims*, 96 GEO. L.J. 461, 475 (2008) (noting that the FDA takes the position that the FDCA impliedly preempts many failure-to-warn claims because the FDA approved the product label based on "balancing the benefits and risks of pharmaceuticals" and required that "the agency [] engage in a complex balancing of interests").

a reasonable physician would not prescribe the drug to any class of patients given its risk-benefit profile, then the FDA has the power to prevent marketing of the drug by denying approval. Thus, the FDA will retain its pre-1962 power to address grave safety concerns. However, by eliminating the FDA's role as merit-regulator, consumers and physicians will have access to more drugs with less time lag.

B. *Disclosure of Clinical Trial Data*

The second part of this proposal requires that the FDA disclose clinical trial data to the public on ClinicalTrials.gov. In addition to actually providing the clinical trial data for all of the phases to the public, the FDA will have the additional task of providing summaries of the clinical trials and results written in non-technical language that is understandable to the public, as well as a more detailed scientific summary that is appropriate for medical professionals. This part of the proposal serves two purposes. First, it provides patients and physicians with access to studies so that they can make independent judgments about the risk profile of drugs. Second, and more importantly, greater transparency promotes information flow and reduces bias. Researchers trying to peddle flawed studies will be deterred, knowing that their data will be available for public scrutiny. Public access to clinical trial data will also counteract biases in publications.

For example, Erick Turner and colleagues analyzed the data of seventy-four antidepressant studies submitted to the FDA between 1987 and 2004.²⁰⁴ They compared the findings of the studies submitted to the FDA to those that were published in the literature and found that close to 50% of the studies failed to show effectiveness.²⁰⁵ Yet, the published literature strongly suggested that the drugs were effective.²⁰⁶ Even more disturbing was the fact that 15% of the published studies reported positive results in spite of the fact that the author's analysis in the original FDA submissions showed negative results.²⁰⁷ Thus, greater access to clinical trial data should lessen publication bias.

Additionally, the rationales supporting disclosure in the SEC context also provide support for mandating disclosure in the FDA context. First, requiring disclosure of all clinical trial data will induce corporate officers, in addition to researchers, to behave more ethically and honestly because they will know that their actions and decisions will

²⁰⁴ Erick H. Turner et al., *Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy*, 358 NEW ENG. J. MED. 252 (2008), available at <http://psychrights.org/research/digest/antidepressants/080117nejmselectivepubofantidepressantdata.pdf>.

²⁰⁵ See *id.* at 256.

²⁰⁶ See *id.*

²⁰⁷ See *id.*

be reviewed.²⁰⁸ Second, requiring disclosure will reduce the costs for doctors, patients, and outside researchers who need the information either to make an informed assessment about the drug or to conduct comparative effectiveness studies.²⁰⁹ Third, greater access to clinical trial data should speed up the dissemination of accurate information regarding the risk-benefit profile of the drug. Timelier information should increase prescriber accuracy. Thus, having better information should enhance physicians' ability to accurately prescribe the drug to the class of patients who can best benefit. Timelier and better access to clinical trial data, as well as post-marketing data, should also allow the market to better assess whether the drug is accurately priced.²¹⁰ Fourth, access to clinical trial data, coupled with the elimination of merit-regulation, furthers the public good.

Elimination of merit-regulation and expanded access to clinical trial data provides an opportunity to reframe public perception to enhance public health. With a properly framed public health campaign, the public should embrace the notion that all drugs have risks and that the risks cannot accurately be assessed in pre-approval process, but the public should also recognize its vital role in reporting data to physicians and health care professionals. Without a vigilant public, the FDA, researchers, and manufacturers will not have an accurate sense of the risk profile of drugs. Thus, it is imperative to educate the public about the limits of pre-approval clinical trials and the necessity of accurate adverse event reporting.

Lastly, it is important to note that Congress has already recognized the need for greater transparency with respect to clinical trials. In 1997, The Food and Drug Administration Act of 1997 (FDAMA) mandated the creation of a registry that would provide data on clinical trials for serious or life-threatening diseases.²¹¹ In order to comply with FDAMA, the FDA, along with the National Institutes of Health, created the ClinicalTrials.gov website. Thus, the vehicle for providing the clinical trial information to the public is already in place.

C. *Enhanced Disclosures of Adverse Events*

The final part of this proposal involves enhanced adverse event reporting. The current regulatory framework is built around

²⁰⁸ See generally Skeel, *supra* note 92.

²⁰⁹ See Mahoney, *supra* note 93, at 1048.

²¹⁰ See Kitch, *supra* note 94, at 773–74.

²¹¹ The FDAMA limited the mandatory registration to Phase II and other advanced trials. It required a plainly written description of the study's purpose, eligibility criteria for participation, location of study sites, and the drug under investigation. Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296.

spontaneous reporting of adverse events.²¹² Manufacturers must report all serious²¹³ and unexpected²¹⁴ adverse reactions to the FDA's Adverse Events Reporting System (AERS) within fifteen days of becoming aware of them.²¹⁵ Manufacturers are also, at quarterly intervals, required to submit reports of all other adverse drug interactions for three years from the date of approval. In essence, the regulations require manufacturers to pass along reports that are received from doctors and other health professionals, but the regulations do not require that manufacturers proactively solicit and obtain information.

Additionally, health care professionals and patients may report adverse reactions to the FDA's MedWatch reporting system.²¹⁶ MedWatch allows health care professionals and consumers to file adverse event reports directly with the FDA via telephone, and to complete the FDA Form 3500 online, or via fax or mail.²¹⁷ This patchwork system undoubtedly means that only a small fraction of adverse reactions are reported to the FDA.

Consequently, the FDA must strengthen disclosure obligations in order to increase the amount and consistency of adverse event reports. Thus, the FDA must require that health care professionals disclose adverse events along with manufacturers. This will provide the FDA with more robust information to evaluate in the post-marketing period. Based on the enhanced post-marketing data, the FDA will be in a better position to exercise its authority to compel label changes or compel market withdrawal of a drug if the risks of the drug do not provide a corresponding therapeutic benefit.

CONCLUSION

Regulating health and wealth is a complex endeavor. While no regulatory model is perfect, the FDA's merit-regulation model is clearly flawed. The power to access the merit of each new drug gives the FDA the power to exercise independent judgment about whether the limited supporting clinical trial evidence justifies approval. The current

²¹² See Parasidis, *supra* note 8, at 980.

²¹³ A serious adverse drug experience results in any of the following outcomes: death, inpatient hospitalization, significant disability, or congenital birth defect. See 21 C.F.R. § 314.80(a) (2012).

²¹⁴ An unexpected adverse drug experience is any adverse reaction "that is not listed in the current labeling for the drug product." *Id.*

²¹⁵ 21 C.F.R. § 314.80(c)(1)(i) (2012).

²¹⁶ See *MedWatch: Reporting Serious Problems to the FDA*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Safety/MedWatch/HowToReport/default.htm> (last updated Sept. 11, 2013).

²¹⁷ See *id.*; FDA Form 3500B, MedWatch Consumer Voluntary Reporting (OMB No. 0910-0291) (expires June 30, 2015), available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM349464.pdf>.

regulatory paradigm is exceedingly slow, requires coordination among many units within the FDA, seems to reward skepticism, and is largely ineffective.

Proposals to reform the FDA are mostly limited to those retaining the FDA's role as merit-regulator. This Article seeks to reframe the debate by advocating for the abandonment of merit-regulation in favor of disclosure. By eliminating merit review of NDA, disclosing clinical trial data, and requiring increased reporting of adverse events, the FDA can better fulfill its mission of protecting the public. Under this proposal, the FDA's role will shift toward facilitating disclosure and reacting to robust post-marketing surveillance data, rather than predicting safety (often inaccurately) based on limited pre-marketing data. In sum, this Article proposes that the FDA and the SEC share similar missions and similar paths.