OKLAHOMA LAW REVIEW

VOLUME 58 SUMMER 2005 NUMBER 2

A PRESCRIPTION FOR DRUG LIABILITY AND REGULATION

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I. Introduction

As recent developments with VIOXX®, childhood anti-depressants, and other prescription drugs have shown, two realities accompany prescription drug use. First, every prescription drug is designed to work miracles for some class of patients. Prescription drugs save patients' lives, enhance their well-being, or provide them with hope where hope was lacking. Second, every prescription drug also has potential side effects, unavoidable negative reactions in a limited number of patients that can be very serious for those who experience them. In a system fraught with winners and losers, fashioning the right balance between regulation and liability involves complicated legal, scientific, and moral issues. Given recent attention to the side effects that patients can experience, now is an appropriate time to revisit the way regulation and liability work within the prescription drug market.

As with all regulatory regimes, the United States Food and Drug Administration (FDA) manages public risk by issuing forward-looking regulations that impose "prescriptive controls on risk-creating conduct

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before"[1] potential injury can occur. What makes the FDA different from other federal agencies is that it must approve the risk-benefit analysis for each product it regulates; each drug must be individually approved before a drug company can make, market, or sell the drug.[2] This drug-by-drug national risk strategy defines the class of patients who are most likely to benefit from a particular drug and assures that doctors are armed with warnings and instructions so they can have a science-based understanding of the known potential risks that each drug can pose. A doctor then assesses a patient's personal risks and decides whether to issue that patient a prescription for a specific drug.

Liability, on the other hand, is a backwards-looking compensation and enforcement mechanism designed to manage private risks. It looks at an individual incident and requires a culpable party to compensate a person it injures *after* the individual injury occurs, thereby providing strong incentives "to control risky behavior in order to avoid or reduce future liability."[3]

Liability falls short in the prescription drug context, because, as the American Law Institute's *Reporters' Study* (*Reporters' Study*) has pointed out, "the tort system is ill-equipped to handle" public risks, particularly in cases requiring "specialized experience in assessing risks and control measures."[4] In these situations, liability works best when it complements the federal regulatory regime by requiring companies to pay compensation when they cause harm by operating outside of its regulatory structure.

This article discusses the central issue of how liability works when a prescription drug manufacturer fully complies with the FDA's exacting regulation by selling, marketing, and labeling prescription drugs with specific FDA approval, yet, because of the nature of prescription drugs, a certain percentage of patients experience significant foreseen and unforeseen side effects. In these situations, jurists have generally taken one of two paths. Some judges, driven by compassion for a plaintiff or their own sense of "justice," reach their own determination that the alleged side effect is more serious than the drug's potential benefit and allow the plaintiff to pursue compensation by claiming that the drug has a design or a failure to warn

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1. 2 AM. LAW INST., ENTERPRISE RESPONSIBILITY FOR PERSONAL INJURY: REPORTERS' STUDY 83 (1991) [hereinafter REPORTERS' STUDY] (stating that the regulatory agencies use their expertise to "determine what risks to control, the level of control, and often the means of control").

2. *See* 21 U.S.C. § 355(a) (2000) ("No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed [with the Food and Drug Administration] is effective with respect to such drug.").

3. REPORTERS' STUDY, *supra* note 1, at 83.

4. *Id.* at 87.

defect.[5] Other judges, adhering to the fundamental principles of tort law, have concluded that there can be no design or warning defect when the FDA has approved a drug's specific design and warnings.[6] These jurists require the manufacturer to have committed an objective wrongful act in order for there to be a basis for liability.[7] The drafters of both the *Restatement (Second) of Torts* and *Restatement of Torts, Third* have determined that the latter path achieves a more accurate and desirable litigation and public policy outcome.[8]

Part II of this article reviews the development and application of the federal regulatory scheme that controls the prescription drug market. Part III addresses the body of law that has been built over the last half century to complement this regulatory regime. Part IV discusses the appropriate liability regime for prescription drugs in this country. Part V examines the key public policy issues that this liability regime raises. Part VI explains the choices available to courts for implementing this liability regime. Part VII raises causation issues that could undermine rational liability laws. Part VIII briefly concludes the article.

II. Federal Regulation of the Prescription Drug Market

A. Development of FDA Authority to Regulate Prescription Drugs

Until the early twentieth century, the federal government generally left the regulation of medicine and public health to the states.[9] As a result, drugs were generally unregulated, thus, leaving many ineffective and potentially harmful drugs on the market.[10] Individuals often made their own choices as to which

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5. *See, e.g.*, Freeman v. Hoffman-La Roche, Inc., 618 N.W.2d 827, 840 (Neb. 2000) (holding that the plaintiff could pursue a design defect claim against the makers of Accutane, a prescription acne medication, and stating that comment k will only apply to prescription drugs on a case by case basis and that, among other factors, the court will consider whether the drug's "benefits justify its risks").

6. *See, e.g.*, Grundberg v. Upjohn Co., 813 P.2d 89, 90 (Utah 1991) ("We hold that a drug approved by the [FDA], properly prepared, compounded, packaged, and distributed, cannot as a matter of law be 'defective' in the absence of proof of inaccurate, incomplete, misleading, or fraudulent information furnished by the manufacturer in connection with FDA approval.").

7. *See, e.g., id.*; Brown v. Superior Court, 751 P.2d 470, 482-83 (Cal. 1988).

8. *See* RESTATEMENT (SECOND) OF TORTS § 402A cmt. k (1965) [hereinafter RESTATEMENT (SECOND)]; RESTATEMENT OF TORTS, THIRD: PRODUCTS LIABILITY § 6 (1998) [hereinafter RESTATEMENT THIRD].

9. *See* John P. Swann, U.S. Food & Drug Admin., History of the FDA, *at* http://www.fda.gov/oc/history/historyoffda/default.htm (last visited Sept. 28, 2005) (adapting sections from A HISTORICAL GUIDE TO THE U.S. GOVERNMENT (George T. Kurian ed., 1998)).

10. States' treatment of drugs varied widely:

> States exercised the principal control over domestically produced and distributed foods and drugs in the 19th century, control that was markedly inconsistent from

drugs to take, as relatively few doctors existed at the time to recommend medications.

The federal government began its effort to standardize drug monitoring and analytical research in 1902, when the Chief Chemist of the Department of Agriculture's Bureau of Chemistry formed the Drug Laboratory; it was a one-man operation with half a desk.[11] A few years later, Congress passed the Pure Food and Drugs Act of 1906,[12] which laid the foundation for modern food and drug law by prohibiting the distribution of mislabeled or adulterated drugs and food in interstate commerce.[13] In 1912, Congress strengthened the law by prohibiting false and fraudulent claims of therapeutic value,[14] and in 1930, it formed the Federal Food and Drug Administration as part of the Bureau of Chemistry.[15]

In 1937, a public health disaster provided the impetus for a tidal shift in federal drug oversight.[16] A well-established pharmaceutical company, Massengill, began selling Elixir Sulfanilamide as treatment for diseases, including strep throat and gonorrhea.[17] The product, which was previously sold as a tablet or in powder form, was manufactured in liquid form in order

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> state to state. . . . Federal authority was limited mostly to imported foods and drugs. Adulteration and misbranding of foods and drugs had long been a fixture in the American cultural landscape, though the egregiousness of the problems seemed to have increased by the late 19th century (or at least they became more identifiable).

Id.

11. *See* Donna Hamilton, U.S. Food & Drug Admin., A Brief History of the Center for Drug Evaluation and Research, *at* http://www.fda.gov/cder/about/history/Histext.htm (last visited Sept. 28, 2005).

12. Pure Food and Drugs Act of 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.

13. *See* Swann, *supra* note 9, at http://www.fda.gov/oc/history/historyoffda/section1.html.

14. Shirley Amendment, Pub. L. No. 62-301, 37 Stat. 416 (1912). Congress enacted this amendment after the Supreme Court of the United States ruled that the Division did not have the authority to seize a product that falsely claimed it could treat cancer. *See* Swann, *supra* note 9, at http://www.fda.gov/oc/history/historyoffda/section2.html.

15. U.S. Food & Drug Admin., *FDA Backgrounder: Milestones in U.S. Food and Drug Law History* (Aug. 2005), *at* http://www.fda.gov/opacom/backgrounders/miles.html [hereinafter *FDA Backgrounder*]. The FDA was transferred from the Department of Agriculture to the Federal Security Agency, the predecessor to the Department of Health, Education, and Welfare, and later to the Department of Health and Human Services. *Id.*

16. *See* Carol Ballentine, *Taste of Raspberries, Taste of Death: The 1937 Elixir Sulfanilamide Incident*, FDA CONSUMER, June 1981, *available at* http://www.fda.gov/oc/history/elixir.html.

17. *See* Paul M. Wax, *Elixirs, Diluents, and the Passage of the 1938 Federal Food, Drug and Cosmetic Act*, 122 ANNALS INTERNAL MED. 456, 458 (1995), *available at* http://www.annals.org/cgi/content/full/122/6/456.

to satisfy popular demand by using diethylene glycol as a medium.[18] Massengill did not realize that diethylene glycol was a deadly chemical known today as antifreeze. The drug killed 107 people — mostly children — before the product was recalled.[19] Because Massengill was not required by the 1906 law to test the safety of the product before marketing it, the FDA could only prosecute the tragedy as a case of mislabeling, as Massengill advertised the drug as an elixir, even though it contained no alcohol.[20]

Congress enacted the Federal Food, Drug, and Cosmetic Act (FDCA) of 1938 to require a manufacturer of a "new drug" to test the product and notify the FDA before bringing the new drug to market.[21] This law, for the first time, required companies to prove the safety of new drugs before placing them into interstate commerce.[22] The FDCA also established the requirement of adequate labeling[23] and began distinguishing between products that required a physician's prescription and those that could be adequately labeled for self-medication.[24]

In 1962, a public health tragedy involving thalidomide, a treatment for morning sickness that resulted in stillbirths and birth defects, led Congress to "fundamentally restructure[] the way in which the FDA regulated new medicines, transforming a system of premarket notification into one that requires individual premarket approval of the safety and effectiveness of every new drug."[25] Specifically, the 1962 Act gave the FDA responsibility for

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18. *See* Ballentine, *supra* note 16.

19. *See id.* (noting that Harold Cole Watkins, the chemist responsible for developing the drug, committed suicide); *FDA Backgrounder*, *supra* note 15.

20. Ballentine, *supra* note 16.

21. Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-399 (2000)).

22. 21 U.S.C. § 355. The 1938 law, while requiring manufacturers to prove the safety of a drug to the FDA before marketing, did not require an evaluation of its effectiveness.

23. *See id.* (stating that a drug would be considered misbranded if its label was "false or misleading in any particular").

24. *See* Michael I. Krauss, *Loosening the FDA's Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, 4 GEO. MASON L. REV. 457, 461 (1996) (stating that the Act included a provision that allowed for discretionary exemptions from labeling requirements, which the FDA interpreted as providing it with the authority to create "a category of 'ethical drugs' that could henceforth be sold only by prescription"). In 1951, the Durham-Humphrey Amendment clarified the legal distinction between prescription and nonprescription drugs. Ch. 578, §§ 1-2, 65 Stat. 648, 648-49 (codified as amended at 21 U.S.C. §§ 333, 353 (2000)).

25. PETER BARTON HUTT & RICHARD A. MERRILL, FOOD AND DRUG LAW CASES AND MATERIALS 13 (2d ed. 1991) (observing the role of the FDA in preventing the outbreak of thalidomide side effects that occurred in Europe from occurring in the United Sates); *see also* Jeffrey E. Shuren, *The Modern Regulatory Administrative State: A Response to Changing Circumstances*, 38 HARV. J. ON LEGIS. 291, 301-03 (2001) (stating that the 1962 Act changed

regulating clinical testing of new drugs, inspecting drug manufacturing facilities, promulgating good manufacturing practices,[26] and requiring manufacturers to report adverse reactions to approved drugs.[27] The FDA also was given oversight responsibilities for prescription drug advertising.[28] In short, the FDA had gained full responsibility for prescribing "the standards of safety and, in some instances, the standards of performance particular products must meet before they reach the public."[29]

Since the 1960s, this framework has remained in place, with Congress making regular improvements as warranted. For example, in response to complaints from patients, doctors, and pharmaceutical companies that the FDA drug approval process was taking too long,[30] Congress enacted the Prescription Drug User Fee Act in 1992, which required manufacturers to pay user fees to the Agency for the evaluation of new drugs.[31] This fee enabled the FDA to hire more reviewers and decreased the wait time for the public to benefit from safe and effective drugs.[32] In fact, the staff at the Center for Drug Evaluation and Research (CDER) increased by over fifty percent between 1980 and 2000.[33]

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the system from pre-market notification to pre-market approval, which effectively "transformed the FDA's role from a reviewer of data to an active participant in the drug development process").

26. *See* Kefauver-Harris Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (codified at 21 U.S.C. §§ 321-399 (2000)). The FDA had delayed approval of the New Drug Application for thalidomide, but FDA officials had not suspected the drug could cause birth defects. *See* FDAReview.org, The Independent Institute, History of Federal Regulation: 1902-Present, *at* http://www.fdareview.org/history (last visited June 25, 2005). The drug, however, was sold in forty-six other countries prior to discovery of its impact, resulting in thousands of newborns with physical deformities. *Id.*

27. *See* Arthur H. Hayes, Jr., *Food and Drug Regulation After 75 Years*, 246 JAMA 1223, 1224 (1981) (noting that oversight of drug advertising was previously undertaken by the Federal Trade Commission (FTC)).

28. *Id.*

29. Richard A. Merrill, *Risk-Benefit Decisionmaking by the Food and Drug Administration*, 45 GEO. WASH. L. REV. 994 (1977), *reprinted in* HUTT & MERRILL, *supra* note 25, at 20.

30. *See* John Henkel, *User Fees to Fund Faster Reviews*, FDA CONSUMER SPECIAL ISSUE, Jan. 1995, *available at* http://www.fda.gov/fdac/special/newdrug/userfees.html.

31. Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, 106 Stat. 4491 (codified at 21 U.S.C. §§ 379g, 379h (2000)).

32. In reauthorizing the Prescription Drug User Fee Act in 1997, Congress found that the Act "substantially reduc[ed] review times . . . ." Food and Drug Modernization Act of 1997, § 101, Pub. L. No. 105-115, 111 Stat. 2296, 2298 (1997). Congress once again reauthorized the Act in 2002. *See* Public Health Security and Bioterrorism Preparedness Response Act of 2002, tit. V, Pub. L. No. 107-188, 116 Stat. 594.

33. *See* Daniel Carpenter & A. Mark Fendrick, *Accelerating Approval Times for New Drugs in the U.S.*, 15 REG. AFF. J. 411, 412 (2004) (on file with author) (finding that the number

The FDA today "administers the most comprehensive drug regulatory system in the world."[34] Its mission is to optimize the risk-benefit tradeoff by only allowing drugs on the market if they are reasonably safe for their intended class of consumers and setting marketing and warning requirements that companies must adhere to in order to sell their products.[35] With a workforce of 9000 people,[36] the Agency regulates more than 150,000 drugs and medical devices.[37] It also conducts more than 16,000 visits per year to facilities that handle FDA-regulated products in order to inspect manufacturers, to review shipments of imported products, and to examine product samples for signs of contamination.[38] CDER, which began as a one-man operation 100 years ago,[39] now employs over 1700 medical doctors, toxicologists, pharmacologists, epidemiologists, chemists, and statisticians.[40]

B. The New Drug Approval Process

The New Drug Application (NDA), the hallmark of the FDA approval process, subjects all prescription drug applications to rigorous formal rule-making review. The NDA enables the FDA to balance carefully the risks and benefits of each prescription drug, to understand the inherent risks, and to determine how to craft warnings for allowing each drug to be used safely and effectively.[41] Where a drug needs to be particularly strong, such as with psychological issues leading to depression, schizophrenia or bi-polar disorder, the FDA may be more tolerant of potentially dangerous side effects, because without those drugs, patients may pose a significant threat to themselves and

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of CDER employees increased from approximately 1100 in 1980 to 1700 in 2000).

34. Bert W. Rein et al., *Addressing the Conflict: FDA vs. Torts*, PHARM. & MED. DEVICE L. BULL., May 2003, at 1, 1, *available at* http://www.lawjournalnewsletters.com/pub/ljn_pharm/3_5/news/141453-1.html (paid access only).

35. "A principal focus of the Food and Drug Administration, apart from safety, is efficacy. Since every drug includes some risks, the Food and Drug Administration regards efficacy as essential — if one is to take risks, he or she should obtain the desired result." Victor E. Schwartz, *Unavoidably Unsafe Products: Clarifying the Meaning and Policy Behind Comment K*, 42 WASH. & LEE L. REV. 1139, 1142 (1985) [hereinafter Schwartz, *Comment K*].

36. Jan Elicker, U.S. Food & Drug Admin., An FDA Overview: Protecting Consumers, Protecting Public Health (Aug. 2004), *at* http://www.fda.gov/oc/opacom/fda101/fda101text.html.

37. U.S. FOOD & DRUG ADMIN., STRATEGIC ACTION PLAN: PROTECTING AND ADVANCING AMERICA'S HEALTH 9 (2003), *available at* http://www.fda.gov/oc/mcclellan/FDAStrategicPlan.pdf [hereinafter FDA STRATEGIC ACTION PLAN].

38. *See* Elicker, *supra* note 36. The agency also has signed cooperative arrangements with many state governments to increase the number of facilities that are checked. *Id.*

39. *See* Hamilton, *supra* note 11.

40. *See* Carpenter & Fendrick, *supra* note 33, at 412.

41. *See generally* 21 C.F.R. pt. 314 (2005).

others.[42] For a drug to be approved, the FDA must determine "that the drug meets the statutory standards for safety and effectiveness, manufacturing and controls, and labeling . . . ."[43]

1. Drug Design

A drug manufacturer starts the approval process by submitting an "Investigational New Drug" (IND) application to the FDA.[44] The FDA uses its considerable scientific expertise to review the application and the drug manufacturer's animal testing of the proposed drug during preclinical research.[45] Only after the FDA approves the IND can a company use the drug in tightly controlled tests with real patients, who agree to participate in the experimental drug program, for gathering data on the drug's clinical safety and efficacy.[46] Upon conclusion of those tests, the manufacturer files a New Drug Application (NDA), detailing the chemistry of the drug, clinical data and patient information, its use in children, reports of adverse reactions, and proposed packaging and labeling, as well as any other pertinent manufacturing

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42. For example, side effects for prescription drugs that may be prescribed for schizophrenia include Neuroleptic Malignant Syndrome, Tardive Dyskinesia, Diabetes Mellitus, and other potentially severe side effects. *See* PHYSICIANS' DESK REFERENCE 2609 (59th ed. 2005) (discussing contraindications, warnings and precautions for Geodon); *id.* at 1742 (for Risperdal); *id.* at 662 (for Seroquel); *id.* at 1899 (for Zyprexa).

43. 21 C.F.R. § 314.105(c). "In fulfilling its mission to monitor and control the safety and efficacy of drugs, the Agency continually walks a razor's edge between two opposing risks — premature approval of dangerous drugs and undue delay in making safe, effective, and medically useful drugs available to the public." Steven R. Salbu, *The FDA and Public Access to New Drugs: Appropriate Levels of Scrutiny in the Wake of HIV, AIDS, and the Diet Drug Debacle*, 79 B.U. L. REV. 93, 96 (1999) (citations omitted).

44. *See* CTR. FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMIN., THE CDER HANDBOOK 7 (Mar. 16, 1998), *at* http://www.fda.gov/cder/handbook/ [hereinafter CDER HANDBOOK]. Generic drugs can use the Abbreviated New Drug Application (ANDA) if it can be based on the pioneer or "listed" drug's approval. 21 U.S.C.A. § 355(j) (West 1999 & Supp. 2005). The generic must be the "bioequivalent" of the pioneer drug, have the same active ingredient, route of administration and dosage, and safe inactive ingredients. *Id.* §§ 355(j)(4)(c), (D), (H).

45. *See* 21 C.F.R. § 312.23. Animal testing is done to determine a drug's potential effect in human beings by using the drug's reaction in animals to identify the chemical compounds at work and assess the toxicity of the drug. *See id.*

46. *See* 21 U.S.C.A. § 355(b)(1); 21 C.F.R. §§ 312.20, 312.21; *see also* Charles J. Walsh & Alyssa Pyrich, *Rationalizing the Regulation of Prescription Drugs and Medical Devices: Perspectives on Private Certification and Tort Reform*, 48 RUTGERS L. REV. 883, 905-07 (1996) (discussing the three phases of human trials).

information.[47] An NDA often spans thousands of pages and describes the impact of the drug in several hundred to several thousand patients.[48]

The CDER's medical officers review the results of the human testing and determine whether the amount of data provided by the manufacturer is sufficient to extrapolate the scientific findings of the test sample to the general population.[49] They can order additional testing or seek the expertise of independent advisory committees.[50] Ultimately, this medical team must approve the prescription drug as being safe and effective for public use.[51]

2. Warnings and Labels

To comply with FDA regulations, warnings must "portray the drug's safety profile with accuracy, balance, and brevity" to help physicians prescribe drugs in ways that maximize a drug's effectiveness and minimize its risks.[52] The label must include basic information, such as a description of the drug, identity of its manufacturer, statement of ingredients, and an expiration date.[53] The label must provide directions for its intended use in the treatment, prevention, or diagnosis of a disease or condition; this information includes any necessary preparation, dosage (recommended, usual, and maximum dosage), and frequency and duration of use.[54] A label also must include a description of any "situations in which the drug should not be used because the risk of use clearly

47. *See* 21 U.S.C.A. § 355(b); 21 C.F.R. §§ 314.50 (providing the required content and format of an NDA), 314.55 (requiring assessment of safety and effectiveness in pediatric subpopulations); *see also* CDER HANDBOOK, *supra* note 44, at 21.

48. *See* Grundberg v. Upjohn Co., 813 P.2d 89, 96 (Utah 1991) (detailing the FDA NDA process).

49. *See* CDER HANDBOOK, *supra* note 44, at 22-23.

50. *See id.* at 23-25. During this process, the manufacturer may submit additional information, as amendments, such as new analysis of previously submitted data or further study to address questions raised during the FDA review. 21 C.F.R. § 314.60; CDER HANDBOOK, *supra* note 44, at 25. FDA investigators may inspect the manufacturer's facilities to verify the accuracy of the practices detailed in the application, to review manufacturing safeguards, and to collect samples for testing. CDER HANDBOOK, *supra* note 44, at 27-28; *see also* 21 C.F.R. pts. 210, 211 (2005) (providing good manufacturing practices for manufacturing, processing, packing, or holding of drugs).

51. *See* CDER HANDBOOK, supra note 44, at 25.

52. W. Kip Viscusi et al., *Deterring Inefficient Pharmaceutical Litigation: An Economic Rationale for the FDA Regulatory Compliance Defense*, 24 SETON HALL L. REV. 1437, 1440 (1994) [hereinafter Viscusi, *Deterring Inefficient Litigation*]. *See generally* 21 C.F.R. pt. 201 (2005) (stating the substantive and stylistics requirements for labels, including that labels and warnings have proper prominence, typeface, and text size).

53. *See* 21 C.F.R. §§ 201.1, 201.10, 201.17, 201.50, 201.51.

54. *See id.* §§ 201.5, 201.55, 201.57.

outweighs any possible benefit."[55] This may include precautionary information regarding any special care needed for the safe and effective use of the drug, such as its use during pregnancy or by children.[56]

Finally, a label must include information on potential side effects, which the FDA breaks down into three categories: (1) "contraindications," where taking the drug would place a patient under severe risk and the patient should be discouraged from taking the drug; (2) "warnings," which are serious risks known to occur in some patients; and (3) "precautions," which are risks that arise less frequently.[57] The manufacturer also must include on the label the steps that should be taken in the event of an adverse reaction, the potential for dependency or abuse, the signs and symptoms of an overdose, and the means of treatment.[58] Unless the FDA grants a specific waiver, the manufacturer must include every element of the extensive disclosures in its labeling.[59]

3. Final FDA Approval

The NDA process is complete only when the Division or Office Director signs an approval action letter allowing the manufacturer to market the drug in the United States.[60] Only eight percent of prospective products submitted to the Agency receive approval and enter the marketplace.[61] The average process for bringing a drug to market takes more than a decade and $800 million.[62]

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55. *See id.* § 201.57(d).

56. *See id.*

57. *Id.* § 201.57(d)-(f).

58. *Id.* § 201.57(g)-(I).

59. *Id.* § 201.58.

60. CDER HANDBOOK, *supra* note 44, at 25. Statutorily, the FDA must approve or reject a New Drug Application (NDA) within 180 days of filing. 21 U.S.C.A. § 355(c)(1) (West 1999 & Supp. 2005); 21 C.F.R. § 314.100(a). In practice, the time frame is much longer because the FDA does not consider an application "filed" until it includes all the required information. Overall, the NDA approval process usually takes one-and-one-half to two years. *See* Ctr. for Drug Evaluation & Research, U.S. Food & Drug Admin., Description of Line Chart: New Drug Application Rates for NDAs Received in FY 1993-2002 and Approved Within 36 Months (Apr. 15, 2003), *at* http://www.fda.gov/cder/present/MedianAPtime/LifeTables/DescLifeTableN2agg9302.htm. Products that treat life-threatening conditions may be eligible for accelerated approval. *See* 21 C.F.R. § 314.500.

61. *See* Lester M. Crawford, Acting Commissioner of the FDA, Speech Before the Mayo Alliance for Clinical Trials Conference (Aug. 26, 2004), *available at* http://www.fda.gov/oc/speeches/2004/mayo0826.html. According to the FDA, the eight percent approval rate is a historic low for the product approvals. *Id.*

62. *See* FDA STRATEGIC ACTION PLAN, *supra* note 37, at 10. The price of developing and bringing a new drug to market has increased rapidly over the past decade. *Id.* (noting that the cost has more than doubled over the past decade); *see also* Henry I. Miller, *Failed FDA Reform*,

C. After-Market Responsibilities

The FDA conducts extensive post-market surveillance to assess whether a drug's real-time safety and efficacy results remain consistent with the risk-balancing decisions made during the NDA process.[63]

This information often comes from epidemiological studies conducted by drug manufacturers, the government, or other entities.[64] These studies examine whether those who take the drug experience previously unknown side effects or whether the instructions for dosage and duration should be amended to achieve the optimal risk-benefit trade-off.[65] In addition, drug companies must report all adverse drug reactions, regardless of whether the company or attending physician believes the adverse illness is related to the drug.[66] Manufacturers also must submit reports on actions taken in response to such adverse drug reactions, as well as any new developments in scientific knowledge on the drug.[67] This responsibility includes the submission of data from post-marketing reports, studies included in scientific literature, and experiences with the drug in other countries.[68] The FDA can enforce these reporting requirements through civil and criminal penalties.[69]

Currently, the FDA monitors more than 10,000 drugs on the market and receives more than 400,000 problem reports a year.[70] Should after-market results indicate that the risk-benefit analysis of the design or warnings are no longer appropriate, the FDA can send warnings to physicians or other health practitioners, require labeling changes, ask the manufacturer to recall a drug, or withdraw the drug's approval altogether.[71]

REGULATION, Summer 1998, at 24, 24 (attributing an increase in cost for new drug development and approval from $359 million to $500 million — in pretax 1990 dollars — between 1990 and 1993, and an increase in the time for approval from 8.1 years to 15.2 years since the 1960s to the "FDA's regulatory zeal").

63. *See generally* 21 C.F.R. § 314.81.

64. *See id.* § 314.81(b)(2)(vi)(a) (requiring "[p]ublished clinical trials of the drug (or abstracts of them), including clinical trials on safety and effectiveness; clinical trials on new uses; biopharmaceutic, pharmacokinetic, and clinical pharmacology studies; and reports of clinical experience pertinent to safety (for example, epidemiologic studies or analyses of experience in a monitored series of patients) *conducted by or otherwise obtained by the applicant*") (emphasis added).

65. *See id.* § 314.81.

66. *See id.* § 314.80(b).

67. *See id.* § 314.80(b), (c).

68. *See id.* § 314.80(b).

69. *See* 21 U.S.C. §§ 332-334 (2000).

70. *See* U.S. FOOD & DRUG ADMIN., CONGRESSIONAL JUSTIFICATION: FY 2003 ANNUAL PERFORMANCE PLAN 2.3.1 (2003), *available at* http://www.fda.gov/ope/fy04plan/2004pp-drugs.html; Elicker, *supra* note 36, at slide 18.

71. *See* 21 C.F.R. § 200.5 (2005) ("[T]he Food and Drug Administration occasionally [is]

In late 2004, "[c]riticism of how the FDA monitors after-market drug safety" grew, and the FDA changed its procedures to allow for even tighter controls.[72] The spark was Merck's withdrawal of VIOXX, a COX-2 Inhibitor that helped mitigate pain from arthritis and minimize the potential for stomach bleeding, which is a common side effect of some other arthritis medications.[73] Studies of after-market results showed that VIOXX taken daily for more than eighteen months could lead to increased risk of heart attack and stroke.[74] After studying these and other scientific data, an FDA expert advisory panel ultimately voted to allow VIOXX to be marketed in the United States with certain restrictions and heightened warnings.[75] In addition, there was increased concern about the effect of certain antidepressants on children, as a number of children who had taken these drugs had committed suicide.[76]

Congress held hearings on both of these issues, and the FDA responded by creating a new independent Drug Safety Oversight Board (Board) to monitor the drug safety of drugs already in the marketplace.[77] The Board is comprised

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required to mail important information about drugs to physicians and others responsible for patient care."); *id.* § 201.200(a)(2) ("The Food and Drug Administration is . . . initiating administrative actions as necessary to require product and labeling changes."); 21 C.F.R. § 7.45(a) (2005) ("[t]he Commissioner of Food and Drugs or designee may request a firm to initiate a recall"); 21 U.S.C. § 355(e) (providing withdrawal authority).

72. Lisa Richwine, *FDA to Create New Drug Safety Board*, REUTERS, Feb. 15, 2005, *available at* http://www.boston.com/business/articles/2005/02/15/fda_to_create_independent_safety_board.

73. *See id.*; Merck & Co., Inc., Patient Product Information, *at* http://www.vioxx.com/rofecoxib/vioxx/documents/english/vioxx_ppi.pdf (Aug. 2004) (explaining that VIOXX is used to relieve arthritis pain); Marc Kaufman, *FDA Panel Opens Door for Return of Vioxx*, WASH. POST, Feb. 19, 2005, at A1 (noting that VIOXX was designed to avoid gastrointestinal problems that were sometime caused by older painkillers).

74. Press Release, Merck & Co., Inc., Merck Announces Voluntary Worldwide Withdrawal of VIOXX® 1 (Sept. 30, 2004), *available at* http://www.vioxx.com/vioxx/documents/english/vioxx_press_release.pdf.

75. *See* Marc Kaufman, *FDA Panel Opens Door for Return of VIOXX*, WASH. POST, Feb. 19, 2005, at A20 (reporting that the thirty-two-member commission banned direct-to-consumer advertising for VIOXX and other COX-2 drugs and required a highlighted black box warning on the bottle label on the risks of heart attacks and strokes).

76. *See, e.g.*, *Hearing Before the H. Subcomm. on Oversight and Investigations*, 108th Cong. (Sept. 23, 2004) (statement of Dr. Robert Temple, Director, Office of Medical Policy, Food and Drug Admin.), *available at* http://www.fda.gov/ola/2004/antidepressant0923.html ("Suicidality, in the context of treating patients with depression and other psychiatric illnesses, has been a genuine concern and a longstanding topic of debate. Whether anti-depressant drug use causes suicidal thinking or behavior in adult or pediatric patients is a critically important question that we must answer in a careful, thoughtful manner.").

77. *Leavitt: Reforms Will Improve Oversight and Openness at FDA*, FDA CONSUMER, May-June 2005 [hereinafter *Leavitt: Reforms*] (quoting Secretary of Health and Human Services Michael Leavitt as saying "The public has spoken and they want more oversight and

of medical experts from the FDA, the Department of Health and Human Services, and other federal agencies, including the Department of Veterans Affairs.[78] The Board also consults with outside medical, patient, and consumer groups. The Board works to educate key audiences about "emerging information for both previously and newly approved drugs about possible serious side effects or other safety risks that have the potential to alter the benefit-risk analysis of a drug, affect patient selection or monitoring decisions, or that can be avoided through measures taken to prevent or mitigate harm."[79] The Board also has the authority to help resolve disagreements over drug safety issues and oversee the development of CDER's drug safety policies.[80]

III. The Development of Prescription Drug Liability

As with the FDA's regulatory structure, the body of tort law that has developed regarding the manufacture and sale of prescription drugs recognizes that harmful side effects are bound to occur because prescription drugs are "unavoidably unsafe."[81] The law also recognizes that, because the FDA uses exacting regulations to tightly manage the public risks associated with these products, the approach for prescription drug liability differs from that of other products.[82]

A. The Law Has Treated Prescription Drug Liability Differently from Liability Stemming from Other Products

In the 1960s, strict products liability emerged for mismanufactured products of all kinds.[83] Under strict liability, as formalized in section 402A of the

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openness . . . . They want to know what we know, what we do with the information, and why we do it. We will address their concerns by cultivating openness and enhanced independence."), *available at* http://www. fda.gov/fdac/features/2005/305_drug.html.

78. U.S. Food & Drug Admin., FDA Fact Sheet: FDA Improvements in Drug Safety Monitoring (Feb. 15, 2005), *available at* http://www.fda.gov/oc/factsheets/drugsafety.html.

79. *Leavitt: Reforms*, *supra* note 77 (stating that the Board will post information on the FDA's website, send regular updates for healthcare professionals, and boil down information for consumer comprehension).

80. *Id.*

81. *See* RESTATEMENT (SECOND), *supra* note 8, § 402A cmt. k.

82. *See* RESTATEMENT THIRD, *supra* note 8, §6 cmt. b ("The traditional refusal by courts to impose tort liability for defective designs of prescription drugs and medical devices is based on the fact that a prescription drug or medical device entails a unique set of risks and benefits. . . . This deference also rests on [the assumption that] governmental regulatory agencies adequately review new prescription drugs and devices, keeping unreasonably dangerous designs off the market.").

83. The first case adopting strict liability was in 1944. *See* Escola v. Coca-Cola Bottling Co., 150 P.2d 436 (Cal. 1944). The doctrine became more widely accepted with Judge

Restatement (Second) of Torts in 1965, courts held product manufacturers liable for injuries caused by defective products even if "all possible care" had been exercised in making, marketing, and selling those products.[84] The law focused solely on the product, assessing whether there was a manufacturing defect, namely that a product was not made in accordance with the manufacturer's own standards.[85] The classic example of a manufacturing defect is the case where a consumer opened a bottle of soda and found mouse droppings and a decomposed mouse that, according to the court's findings, were in the bottle before liquid was added during the manufacturing process.[86] If such a manufacturing defect were to cause harm, the plaintiff could sue under strict liability and would not have to satisfy the requirements of traditional negligence or warranty actions. Liability would attach even if the manufacturer had acted reasonably in making the product.[87] Gradually, "strict liability" extended beyond manufacturing cases to claims brought on the basis of failure to warn or defective design.[88] Courts initially struggled with applying strict liability in these types of cases.[89]

The *Restatement (Second)*, in comment k of section 402A, avoids confusion for design and failure to warn defects with respect to prescription drugs. Comment k states that it would be unfair to apply strict liability to design defects "in the field of drugs" because vaccines and prescription drugs are "incapable of being made safe for their intended and ordinary use."[90] For

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Traynor's decision in *Greenman v. Yuba Power Prods., Inc.*, in which he wrote that a "manufacturer is strictly liable in tort when an article he places on the market, knowing that it is to be used without inspection for defects, proves to have a defect that causes injury to a human being." 377 P.2d 897, 900 (Cal. 1963).

84. RESTATEMENT (SECOND), *supra* note 8, § 402A.

85. *See generally* RESTATEMENT (SECOND), *supra* note 8, § 402A.

> A careful examination of the Appendix to Section 402A of the *Restatement* and discussions by the eminent Professor John W. Wade, who later became the reporter for the *Restatement* itself, show that all of the cases that were considered involved *mismanufactured* products — contaminated food products or products with construction defects. These were cases where products contained foreign objects, were missing important parts, or were not assembled in accordance with the manufacturer's own design plans.

Schwartz, *Comment K*, *supra* note 35, at 1139 (citations omitted).

86. Shoshone Coca-Cola Bottling Co. v. Dolinski, 420 P.2d 855 (Nev. 1966).

87. See RESTATEMENT (SECOND), *supra* note 8, § 402A(2)(a) (stating that the rule applies even though "the seller has exercised all possible care in the preparation and sale of his product").

88. *See, e.g.*, Cronin v. J. B. E. Olson Corp., 501 P.2d 1153 (Cal. 1972).

89. *See generally* John W. Wade, *On Product "Design Defects" and Their Actionability*, 33 VAND. L. REV. 551 (1980) [hereinafter Wade, *"Design Defects"*].

90. RESTATEMENT (SECOND), *supra* note 8, § 402A cmt. k. Dean Prosser, reporter for the *Restatement (Second)*, chose to handle prescription drug liability in a comment rather than a

example, as the *Restatement (Second)* observes, the Pasteur treatment of rabies can lead to serious and damaging side effects: "[s]ince the disease itself invariably leads to a dreadful death, both the marketing and the use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve."[91]

The *Restatement (Second)* applies this premise to all prescription drugs.[92] It states that while these products are "[u]navoidably unsafe," when "accompanied by proper directions and warning," they are not "*unreasonably* dangerous."[93] In so doing, the *Restatement (Second)* offers a fault-based liability system for design defects for prescription drugs and vaccines.[94] If a drug manufacturer meets a reasonable standard of care for both design and labeling, the product is not defective.[95] Consequently, if a person experiences a side effect caused by such a non-defective drug, that person will have a claim against the manufacturer only if the manufacturer violated some other liability theory,[96] namely negligence, fraud, or express warranty.[97]

B. Judicial Reaction to Comment k

Courts have overwhelmingly agreed with the premise of comment k, that is, that the "unreasonably dangerous" test and not strict liability should be applied to design defects for unavoidably unsafe prescription drugs.[98] By the

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separate section. *See* Brown v. Superior Court, 751 P.2d 470, 475 (Cal. 1988).

91. RESTATEMENT (SECOND), *supra* note 8, § 402A cmt. k.

92. *Id.* ("It is also true in particular of many new or experimental drugs as to which, because of lack of time and opportunity for sufficient medical experience, there can be no assurance of safety, or perhaps even of purity of ingredients, but such experience as there is justifies the marketing and use of the drug notwithstanding a medically recognizable risk.").

93. *Id.*

94. *Id.*

95. Schwartz, *Comment K*, *supra* note 35, at 1141.

96. *See generally id.*

97. Express warranty is "based on the fact that the defendant made a specific representation about a product's safety; plaintiff relied on that representation, and it turned out to be untrue." Victor E. Schwartz, *Violation of Express Warranty: A Useful Tort that Must Be Kept Within Rational Boundaries*, 3 PRODS. LIAB. L.J. 147, 148 (1992) [hereinafter Schwartz, *Express Warranty*].

98. "Comment k has been adopted in the overwhelming majority of jurisdictions that have considered the matter." Brown v. Superior Court, 751 P.2d 470, 476 (Cal. 1988) (citing DeLuryea v. Winthrop Labs., 697 F.2d 222, 228-29 (8th Cir. 1983); Basko v. Sterling Drug, Inc., 416 F.2d 417, 425-26 (2d Cir. 1969); Stone v. Smith, Kline & French Lab., 447 So. 2d 1301, 1303-04 (Ala. 1984); Gaston v. Hunter, 588 P.2d 326, 338-41 (Ariz. Ct. App. 1978); Chambers v. G.D. Searle & Co., 441 F. Supp. 377, 380-81 (D. Md. 1975); Johnson v. Am. Cyanamid Co., 718 P.2d 1318, 1323 (Kan. 1986)). "We are aware of only one decision that has applied the doctrine of strict liability to prescription drugs." *Id.* (citing Brochu v. Ortho Pharm. Corp., 642 F.2d 652, 654-57 (1st Cir. 1981)).