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Institute for Civil Justice

Economic Effects of Product Liability and Other Litigation Involving the Safety and Effectiveness of Pharmaceuticals

Steven Garber

The research reported here was conducted in the RAND Institute for Civil Justice, a program of RAND Justice, Infrastructure, and Environment.

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Preface

Many people are concerned about the economic effects of product liability in the United States, and there has been an active policy debate about this issue for several decades. Liability effects on the economic performance of the pharmaceutical industry have played a leading role in this debate. More recently, concerns have grown about other kinds of litigation in which drug safety and effectiveness are central issues. Such other safety- and effectiveness-related litigation includes criminal and civil complaints brought by the U.S. Department of Justice and lawsuits brought by state attorneys general and private plaintiffs under state consumer protection acts and other causes of action.

This monograph examines the economic incentives of pharmaceutical companies stemming from product-liability and other forms of litigation and considers effects on company decisions affecting product safety, effectiveness, availability, prices, and the mix of research and development. The emphasis, however, is on product safety and effectiveness. It should be of interest to policymakers and policy analysts who seek to understand the economic effects of pharmaceutical product-liability and related litigation as well as to legal practitioners and policy advocates as they formulate their policy arguments.

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representatives of different interests to debate alternative solutions to policy problems. Institute for Civil Justice research is supported by pooled grants from a range of sources, including corporations, trade and professional associations, individuals, government agencies, and private foundations. It disseminates its work widely to policymakers, practitioners in law and business, other researchers, and the public. In accordance with RAND policy, all its reports are subject to peer review. Its publications do not necessarily reflect the opinions or policies of its research sponsors.

Questions or comments about this monograph should be sent to the author, Steven Garber (Steven_Garber@rand.org). For more information about the Institute for Civil Justice, see <http://www.rand.org/jie/research/civil-justice.html> or contact the director at icj@rand.org.

Contents

Preface	iii
Figure and Tables	ix
Summary	xi
Acknowledgments	xvii
Abbreviations	xix

CHAPTER ONE

Introduction	1
---------------------------	---

CHAPTER TWO

Conceptual Framework for the Analyses	5
Positive Analysis: Effects of Liability Exposure on Company Decisions and Economic Outcomes ...	6
Company Decisions and Economic Outcomes	7
Conceptualizing Company Decisionmaking	9
What Determines Whether Companies Respond to Liability Exposure?	10
What Kinds of Conclusions Are Possible from the Positive Analytic Approach?	10
Normative Analysis: Economic Efficiency of Effects of Liability Exposure	11
Economic Efficiency	11
Identifying Sources of Inefficiency	14

CHAPTER THREE

The Legal and Institutional Settings	15
Food and Drug Administration Regulation	15
Preapproval Regulations	15
Post-Market Regulations	16
Product-Liability Law for Prescription Drugs	17
Manufacturing Defects	18
Design Defects	18
Warnings Defects	19
Regulatory Compliance Defenses (RCDs)	19
Other Legal Issues and Practices	20
Personal-Injury Causation	20
Class Actions Alleging Personal Injuries	21
Class Actions Alleging Financial Injuries	21
Judicial Gatekeeping of Expert Evidence	21
U.S. Supreme Court Decisions on Sizes of Punitive Damages	22

Medical Monitoring Claims.....	23
Congregation and Coordination of Related Lawsuits.....	24
Settlements of Mass Torts.....	25
CHAPTER FOUR	
Pharmaceutical Mass Torts During the 1990s and 2000s	27
Mass Torts Resulting in Especially Large Payouts by Defendants.....	28
Fen-Phen Diet Pills.....	28
Baycol.....	31
Rezulin.....	32
Vioxx.....	32
Hormone Replacement Therapies—Premarin, Provera, and Prempro.....	35
Zyprexa.....	36
Mass Tort Attempts Resulting in Substantially Smaller Payouts by Defendants.....	37
Norplant.....	38
Childhood Vaccines and Autism.....	39
Other Mass Tort Attempts That Have Largely Failed for Plaintiffs.....	42
Summing Up.....	42
Mass Drug-Related Injuries.....	42
Mass Torts.....	43
Financial Incentives to Avoid Liability.....	43
Roles of Punitive Damages.....	44
Controversies About Injury Causation.....	44
Transaction Costs of Unsuccessful Mass Tort Attempts.....	45
CHAPTER FIVE	
Preemption of Pharmaceutical Failure-to-Warn Claims	47
Federal Preemption Law.....	47
Purported Economic Effects of Failure-to-Warn Claims.....	48
Economic Arguments Supporting Preemption.....	53
Economic Arguments Opposing Preemption.....	59
Preemption of Failure-to-Warn Claims for Generic Drugs.....	60
Would Failure-to-Warn Litigation Pass a Social Cost-Benefit Test?.....	61
Sources of Confusion in the Preemption Debate.....	61
The Overall Economic Efficiency of FTW Litigation Is Unknown.....	62
CHAPTER SIX	
Incentives Stemming from Other Litigation Affecting Safety and Effectiveness	63
Actions Brought by the U.S. Department of Justice.....	64
State Consumer Protection Acts—Background and Controversies.....	65
Safety- and Effectiveness-Related Litigation Brought by State Attorneys General.....	68
Safety- and Effectiveness-Related Financial-Injury Litigation Brought by Private Parties.....	69
Shareholder Suits Pertaining to Pharmaceutical Safety and Effectiveness.....	71
Summing Up.....	73

CHAPTER SEVEN

In Conclusion	77
Major Legal Developments Since 1990.....	78
Product Liability for Personal Injury	78
Other Litigation Pertaining to Drug Safety and Effectiveness	78
Approach to Policy Improvement	78
Liability-Based Incentives Encouraging Inefficient Manufacturer Behavior.....	79
Incentives to Overwarn	79
Punitive Damages.....	79
Liability-Based Incentives Encouraging Efficient Manufacturer Behavior.....	79
Compliance with FDA Regulations	79
Honest and Complete Public Reporting of Risk Information.....	80
Liability-Based Incentives Encouraging Inefficient Behavior by Plaintiffs' Lawyers and Consumers.....	80
Competition Among Plaintiffs' Attorneys to Lead Mass Tort Attempts.....	80
Litigation and Consumer Compliance with Prescribed Therapies.....	80
Product-Liability Preemption for Medical Products.....	81
Issues to Study and Developments to Monitor	81
Final Remarks	82
References	85

Figure and Tables

Figure

2.1. Conceptual Framework for Inferences About Economic Outcomes	7
--	---

Tables

2.1. Economic Outcomes and Major Associated Decisions of Pharmaceutical Companies ...	8
4.1. Number of Pending Diet Pill Lawsuits Reported to the SEC by AHP/Wyeth, 1998–2000	29
5.1. Claimed Economic Effects of Pharmaceutical Failure-to-Warn Liability in FDA Preemption Debate	49

Summary

Product safety is a major policy concern in the United States, and potentially dangerous products are regulated by several federal agencies. Moreover, markets can penalize manufacturers and sellers of hazardous products by reducing demand. To further promote product safety, U.S. product sellers are also subject to product liability, which in some circumstances imposes legal obligations to compensate people injured by their products and thereby gives sellers additional financial incentives to reduce product hazards. Many product-liability proponents and policymakers point to compensation of injured product users as another worthy social goal served by product liability.

Critics argue, however, that compensation for injuries through product liability is socially undesirable. One reason is that legal disputing uses up many more scarce resources per dollar transferred than other compensation mechanisms. Moreover, product-liability critics argue that company responses to incentives from product liability have unintended and socially undesirable effects on economic outcomes, such as undermining product safety and effectiveness, discouraging innovation, increasing product prices, and driving good products off the market. In short, product-liability critics emphasize socially undesirable economic effects.

Prescription drugs are often in the forefront in public and scholarly debates about the economic effects of product liability. Economic effects of pharmaceutical product liability, however, are surprisingly difficult to analyze empirically, and there is little direct empirical knowledge about them. To further complicate matters, other forms of legal liability also penalize drug companies financially for acts affecting drug safety and effectiveness and as a result are likely to affect company decisions and economic outcomes.

Despite these difficulties, this monograph analyzes economic effects of several kinds of legal liability for pharmaceutical companies with an emphasis on drug safety and effectiveness. In addition to product liability for personal injuries, the monograph considers three other types of litigation related to safety and effectiveness that often allege deceptive marketing and/or illegal (*off-label*) promotion of drugs for uses not approved by the U.S. Food and Drug Administration (FDA):

- Civil and criminal actions brought by the U.S. Department of Justice (DOJ) under the federal Food, Drug, and Cosmetics Act, the federal False Claims Act (FCA), or both
- Civil and criminal actions brought by state attorneys general (AGs) under state consumer protection acts (CPAs) and/or other causes of action

- Civil actions alleging financial injury brought by private plaintiffs under state CPAs and/or other causes of action.¹

Analytic Approach

The analysis comprises several components: developing a conceptual framework of company decisionmaking in response to liability exposure, reviewing and assessing previous empirical studies of economic effects of pharmaceutical product liability, examining the histories of several mass (product-liability) torts since 1990, reviewing instances of each of the other types of liability, characterizing how company decisionmakers are likely to perceive the connections between their decisions and potential future liability costs, and drawing inferences about how potential liability costs are likely to affect company decisions and economic outcomes. Finally, the monograph identifies socially desirable and undesirable outcomes of pharmaceutical liability and encourages policymakers to consider policy reforms to reinforce desirable outcomes and attenuate undesirable ones in the future.

A major challenge in connecting economic outcomes to liability is that, with few exceptions, outsiders cannot observe key company decisions or their consequences for economic outcomes. In response, much of the analysis relies on (1) developing empirical information about companies' liability costs resulting from different company actions,² (2) applying well-established perspectives on decisionmaking to draw inferences about likely company responses to liability induced incentives, and (3) assessing the social consequences of such responses.³

Conceptual Framework

Drawing reliable inferences about company responses to liability exposure requires a suitable conceptual foundation addressing company decisionmaking, as summarized here. Economic outcomes result from decisions made by drug companies seeking to maximize future profits, which can be reduced by future liability costs. These costs may be revealed only years after decisions are made and thus can be extremely uncertain. Decisions depend on company decisionmakers' perceptions about their incentives stemming from liability—equivalently, the perceived financial implications of different courses of action. When making decisions, then, companies try to anticipate their future liability environments, presumably in large measure on the basis of fairly recent history.

Several kinds of drug-company decisions affect drug safety and effectiveness. For example, companies choose a drug's design or physical properties as well as how and how extensively to study safety and effectiveness. Moreover, a drug's safety and effectiveness depend on who takes it and how, which depend on company decisions such as (1) the medical purposes for which the drug is intended, (2) recommended dosage levels, (3) product warnings, (4) what

¹ The monograph also considers civil litigation brought by drug company shareholders, which seems insubstantial relative to the other kinds of liability.

² Sources of empirical information include drug company reports to shareholders, litigation reports, articles in law and medical journals, and print and online reports from popular, legal, and trade news services.

³ Statistical analyses and case studies are alternatives to this inferential approach. However, as explained in the monograph, these other approaches are not promising for the purposes of this monograph, namely, characterizing the overall or typical economic effects of liability.

information is reported to the FDA, and (5) how products are marketed and promoted to prescribers and consumers.

Evaluating the Social Desirability of Economic Effects

The monograph evaluates the social desirability of economic effects of liability in terms of economic efficiency, which can be thought of as what the pharmaceutical industry contributes to the aggregate economic well-being of U.S. residents. Economic efficiency can be improved in three ways, namely (1) increasing the population-level health benefits of pharmaceuticals, (2) decreasing social costs of drug-related injuries, and (3) decreasing the resource or “transaction” costs of legal disputing.

Thus, assessing the social desirability of different liability policies raises three questions: How do incentives from the liability system affect the health benefits of prescription drugs? How do these incentives affect the social costs of drug-related injuries? And what is the social cost of the resources used in disputing liability claims, such as the time of lawyers, experts, judges, and jurors?

Case Studies of Mass Torts

The new empirical content of the monograph pertaining to product liability focuses on incentives of drug companies to avoid mass torts, which are fairly common for prescription drugs and can involve extremely high costs for drug companies. The analysis considers six mass torts since 1990 that resulted in indemnity payments of roughly \$1 billion or more (Fen-phen diet pills, Baycol, Rezulin, Vioxx, hormone replacement therapies, and Zyprexa) as well as four other mass torts that resulted in considerably smaller aggregate payouts.

Key Findings

Based on Review and Assessment of Previous Empirical Literature and New Empirical Analysis, What Does the Analysis Reveal About Economic Effects of Pharmaceutical Liability?

Evidence from Previous Studies

The monograph reviews empirical studies of economic effects of pharmaceutical product liability.⁴ To provide an overview of the state of the policy debate concerning product liability, the monograph reviews arguments about economic effects set out in *amici* briefs filed with the U.S. Supreme Court in the case of *Wyeth v. Levine*. The issue before the court in this case was whether state product-liability claims against drug manufacturers alleging failure to warn of potential injuries—which comprise the lion’s share of pharmaceutical product-liability claims—are preempted by federal law. In March 2009, the court ruled that such claims are not preempted.

Those who supported preemption (opponents of product liability) argued that pharmaceutical product liability has reduced product availability, increased drug prices, discouraged innovation, and affected drug safety in two economically inefficient ways. Surprisingly, preemption supporters paid little attention to the transaction costs of litigation.

⁴ It appears that there are no analogous studies concerning the other forms of liability considered in this monograph.

Those who opposed preemption argued that product-liability litigation uncovers new information about drug hazards and deters “questionable practices” (socially undesirable corporate behavior). Surprisingly, preemption opponents paid little attention to the role of product liability in leading to withdrawals—with or without FDA intervention—of drugs that many in the medical community viewed as too dangerous in relation their health benefits to remain on the market.

What is the evidence concerning these arguments? Most importantly, there is scant empirical evidence to support the claims asserted on either side of the debate, and the literature provides little reliable information about common or typical economic effects of pharmaceutical product liability.

There is some empirical support for the view that product liability *can* have undesirable economic effects, but almost no support for sweeping claims about product liability *often having* such effects. Literature provides substantial evidence that product liability caused the withdrawals of Bendectin in 1983, some vaccines during the 1980s and 1990s, and the contraceptive Norplant in 2002. There is also strong evidence that sharp increases in the prices of some vaccines during the 1980s were caused by product liability, but the reliability of econometric evidence suggesting that product-liability exposure increased the prices of other kinds of drugs (in 1990) is equivocal. It appears impossible to develop direct empirical evidence about the effects of product liability on innovation, although there is a fairly strong qualitative basis for inferring that product liability has been a major factor in discouraging efforts to develop new contraceptives. The only econometric study of product liability and pharmaceutical innovation focused on vaccines and found that decreased liability increased efforts to develop new vaccines, but it also concluded that these increases probably undermined economic efficiency.

Critics of liability have made two claims about product liability reducing product safety. The first is that excessively detailed and extensive product warnings—so-called “overwarning”—interfere with effective drug prescribing and thereby undermine safety and effectiveness. That claim is controversial within the medical community, and there is no direct empirical evidence about it. However, there is some indirect supporting evidence from FDA surveys and focus groups with physicians conducted in 1992. The second claim is that the FDA’s safety standards are higher than efficient levels and, thus, liability-induced increases in safety would undermine economic efficiency; this claim is plausible but entirely theoretical.

The literature also provides limited evidence to support the claims of proponents of product liability. For example, studies have demonstrated that litigation has uncovered important, safety-related information previously unknown to the FDA, prescribers, and the public. In principle, this information could provide a basis for FDA actions to improve the safety with which particular drugs are used or to improve FDA policies more broadly. There appears to be no systematic empirical information about such FDA responses, however. There is also a substantial theoretical basis for expecting that exposing “questionable practices” by drug companies will deter some future instances of such practices; again, however, there is no direct empirical information bearing on this hypothesis.

New Empirical Analyses

Employing the conceptual framework described above, the monograph also considers what might be reasonably inferred about economic effects based on new empirical information. Consider the different kinds of liability in turn, beginning with product liability for personal injuries.

The potential cost of a mass tort to a drug company is in the billions of dollars. Such a large financial threat almost certainly commands attention from company decisionmakers and leads them to consider ways to reduce the likelihood of a mass tort attempt involving one of their drugs, the company's likely cost if such an attempt is made, or both. Company decisionmakers are likely to be willing to sacrifice substantial amounts in profits in the near term to avoid behavior that they view as substantially increasing their future exposure to mass torts.

Lawsuits brought by DOJ have resulted in several settlements of \$500 million or more, with at least a few exceeding \$1 billion. Such litigation will tend to discourage behavior that DOJ investigates and sanctions such as off-label promotion and/or deceptive marketing. Several actions brought by state AGs have been settled for tens of millions of dollars, and there have also been jury verdicts of roughly \$250 million and \$325 million. Many of the state AG suits are likely to fortify deterrence effects of DOJ actions.

It is more difficult to gauge the financial threat perceived by drug company decisionmakers from private lawsuits. Many of these financial-injury lawsuits are brought by third-party payers alleging that they would not have willingly paid as much as they did for particular drugs were it not for illegal or deceptive behavior by drug companies. A key unknown about the future financial threats to drug companies—and the likelihood that these threats will substantially alter future company decisions—is the frequency with which financial injury lawsuits brought as class actions will be certified.

Direct Empirical Evidence: Summary

In sum, *there is little direct empirical evidence concerning the economic effects of product liability or the other forms of liability considered in this monograph.* Most of the direct evidence available about product liability pertains to particular drugs, and almost all of that evidence pertains to events that occurred a decade or more ago. Moreover, there appears to be essentially no direct empirical information about economic effects of the other forms of pharmaceutical liability considered in this monograph. Policymakers should, then, be wary of broad claims about economic effects of pharmaceutical liability, including generalizations based on anecdotes or examples.

Implications for Public Policy

The overall economic effects of liability—and comparison of total social costs and benefits—are the fundamental issue only when the policy question is whether to eliminate liability. This is rarely the policy question despite the counterexample of *Wyeth v. Levine* in the case of product-liability, failure-to-warn litigation.

Previous studies and new analyses contained in this monograph offer some, albeit limited, guidance about how policy changes designed to alter company incentives could improve the economic effects of liability. The liability exposure of drug companies creates both socially desirable and socially undesirable incentives for drug companies.

Features of the liability system create socially desirable incentives, including:

- **Incentives to comply with FDA regulations.** In most states, compliance with FDA regulations does not shield companies from liability, while evidence of failure to comply can be extremely costly to them. Imposing liability costs for regulatory noncompliance tends to encourage compliance. With the possible exception of restrictions on truthful off-label promotion, increasing compliance with major FDA regulations—requiring, for example, post-market clinical studies and honest reporting to the FDA—seems likely to promote economic efficiency.
- **Discovery of safety-related information.** Liability litigation sometimes uncovers evidence of company failures to provide safety-related information to the FDA, prescribers, and consumers. Examples include withholding or distorting information about the frequency and severity of injuries and withholding the results of selected clinical trials. Discovering such information in the course of litigation and penalizing it through legal liability tend to discourage it.

Other features of the liability system create socially undesirable incentives, including:

- **Incentives to overwarn.** Product-liability doctrine holds firms liable for failure to warn, as contrasted with, for example, failure to provide warnings that best promote public health through prescribing decisions and consumer compliance with their doctors' prescriptions.
- **Vague standards for punitive damages.** Punitive damages are likely to loom large in the minds of company decisionmakers. Under the laws of many states, the circumstances under which punitive damages are available are described as actions that are “outrageous,” “oppressive,” “malicious,” and so on. The vagueness of these standards can leave corporate decisionmakers with great uncertainty about what behavior is required on their parts to avoid punitive damages and, as a result, can deter socially desirable corporate behavior.

Policymakers are encouraged to identify and implement changes in the liability environment that would alter company incentives and thereby lessen socially undesirable economic effects while maintaining or strengthening the desirable ones. No silver bullets are likely to be found. In view of the apparently high social stakes, however, identifying and implementing such policy changes could be well worth the considerable efforts required. This monograph offers information that could aid such efforts.

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Any remaining shortcomings are the sole responsibility of the author.

Abbreviations

AAJ	American Association for Justice
<i>ADRLR</i>	<i>Andrews Drug Recall Litigation Reporter</i>
AE	adverse (drug-related) event
AG	attorney general
AHP	American Home Products
ALI	American Law Institute
<i>APLR</i>	<i>Andrews Pharmaceutical Litigation Reporter</i>
ATLA	Association of Trial Lawyers of America
CPA	consumer protection act
DOJ	(United States) Department of Justice
DPT	diphtheria, pertussis, tetanus (combination vaccine)
DTC	direct-to-consumer (advertising of pharmaceuticals)
FCA	(federal) False Claims Act
FDA	(U.S.) Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act (of 2007)
FDCA	Food, Drug, and Cosmetic Act
FTC	(U.S.) Federal Trade Commission
FTW	failure to warn
HCSC	Health Care Services Corp
HRT	hormone-replacement therapy
ICJ	(RAND Corporation) Institute for Civil Justice
IOM	Institute of Medicine (of the National Academies)
MDL	(federal court) multidistrict litigation

MMR	measles, mumps, and rubella (vaccine)
NCAS	Nationwide Class Action Settlement (of Fen-phen litigation)
NCVIA	National Childhood Vaccine Injury Act
OPV	oral polio vaccine
PhRMA	Pharmaceutical Research and Manufacturers of America
PLAC	Product Liability Advisory Council, Inc.
PPH	primary pulmonary hypertension
PPL	pharmaceutical product liability
R&D	research and development
RCD	regulatory compliance defense
RICO	Racketeer Influenced and Corrupt Organizations Act
Rx	prescription
SCA	securities class action
SDS	shareholder derivative suit
SEC	(U.S.) Securities and Exchange Commission
SGA	second-generation atypical
SSRI	selective serotonin reuptake inhibitor (a class of antidepressant drugs)
TPP	third-party payer (for pharmaceuticals)
USCC	U.S. Chamber of Commerce
VHD	valvular heart disease
VICF	Vaccine Injury Compensation Fund
VICP	Vaccine Injury Compensation Program
WHI	Women's Health Initiative

Introduction

In theory, product liability can increase product safety by strengthening incentives for manufacturers or other product sellers to increase their levels of precaution (or “care”) in designing, manufacturing, labeling, and promoting their products. The economic effects of product liability, and many other forms of legal liability, play a prominent role in debates about civil justice policy, perhaps no more so than for pharmaceuticals. The purpose of this study is to improve understanding of the economic effects of several kinds of litigation brought against pharmaceutical companies in which a central issue is the safety and/or effectiveness of particular prescription pharmaceuticals.

Regarding product liability, the monograph reviews case histories of several pharmaceutical mass torts that plaintiffs’ attorneys have attempted to develop since 1990 and for which the basic contours of their resolutions are now apparent. Some of these attempts have been successful from the plaintiffs’ point of view in that they have resulted in indemnity payments by defendant companies to claimants and their lawyers of roughly \$1 billion or more. Other attempts have been much less successful from the plaintiffs’ point of view in that they have resulted in much smaller total indemnity payments.

This monograph examines economic effects of personal-injury product-liability litigation as well as other forms of civil litigation that may substantially alter drug manufacturers’ incentives when they make decisions affecting the safety and effectiveness of their prescription drugs. I refer to these other forms of litigation as *other safety- and effectiveness-related litigation* or, equivalently, *related litigation*. The related litigation of interest for the purposes of this monograph comprises legal actions against pharmaceutical companies in which the central allegations pertain to the safety and/or effectiveness of particular drugs.

In particular, I consider the following kinds of “related” (to product liability) legal claims asserted against pharmaceutical manufacturers: (1) selected¹ criminal and civil complaints brought by the U.S. Department of Justice (DOJ) alleging violations of the Food, Drug, and Cosmetics Act (FDCA) or the False Claims Act (FCA); (2) selected lawsuits brought by state attorneys general (AGs) under their states’ consumer protection acts (CPAs); other statutes or common law causes of action; (3) selected class-action and other lawsuits brought by private parties for financial injury under states’ CPAs, other statutes, or common law causes of action;

¹ In particular, only some claims brought against pharmaceutical companies by the DOJ under these statutes are safety or effectiveness related, and the analysis focuses on these claims. Similar comments apply to the other types of related litigation considered in the monograph. Much of the litigation brought against drug companies are outside the scope of this study because neither product safety nor product effectiveness is a central issue. Examples of litigation not considered in this study are antitrust and patent litigation as well as litigation alleging kickbacks and overcharging U.S. government drug purchasers.

and (4) securities class actions (SCAs) and shareholder derivative lawsuits alleging failure to disclose to shareholders (a) health risks of particular prescription drugs or (b) deceptive marketing or illegal promotion. For ease of exposition, I use the term *liability* to refer to product liability and these four other types of legal liability.

The monograph is organized as follows. The next chapter presents the conceptual foundations of the analyses. More specifically, that chapter explains perspectives on how liability exposure affects economic outcomes through decisions made by pharmaceutical companies, why inference is required to draw conclusions about economic effects, and what it means and why it is appropriate to focus on economic efficiency as the normative criterion for assessing economic effects.² The chapter also discusses why alternative analytic approaches are unpromising.

Chapter Three provides legal and institutional background for the subsequent discussions and analyses. More specifically, that chapter discusses pertinent aspects of regulation by the U.S. Food and Drug Administration (FDA), the basics of product-liability law for prescription pharmaceuticals, and other legal and institutional considerations such as establishing injury causation, personal- and financial-injury class actions, judicial gatekeeping of expert evidence, U.S. Supreme Court decisions on the permissible sizes of punitive damages awards, claims for medical monitoring, congregation and coordination of related lawsuits, and forms of mass tort settlements.

Chapter Four contains case histories of pharmaceutical mass torts that seem to have largely played out by the fall of 2011. These include mass torts with relatively large total indemnity payments—namely, Fen-phen diet pills, Baycol, Rezulin, Vioxx, hormone replacement therapies and Zyprexa³—and mass tort attempts that have not been nearly as successful from the plaintiffs' point of view—namely, Norplant, childhood vaccines and autism, Meridia, and Serzone. The chapter concludes with an analysis of likely effects of pharmaceutical product-liability (PPL) litigation on company decisions and discussions of the roles of injury-causation controversies, punitive damages, and transaction costs of litigation.

Chapter Five discusses preemption (i.e., prohibition) under federal law of state-law PPL claims emphasizing failure to warn (FTW), which comprise most of PPL litigation. In that chapter, I exploit the fact that many *amici* briefs discussing purported economic effects of PPL were filed in support of both the petitioner and respondent in *Wyeth v. Levine*, a preemption case decided by the U.S. Supreme Court in March 2009. I review and assess claims about economic effects of PPL in these *amici* briefs, the sources they cite, and other sources. This chapter also considers preemption of product-liability claims against manufacturers of generic versions of branded drugs, which was the subject of the U.S. Supreme Court's June 2011 decision in *Pliva v. Mensing*. Chapter Five concludes by considering whether product liability for prescription pharmaceuticals would likely pass or fail a social cost-benefit test (equivalently, whether it is likely to enhance or undermine economic efficiency).

Chapter Six describes the four types of related litigation listed above and offers several examples of particular lawsuits and allegations for each of the four types. The chapter concludes by considering whether drug company decisions are likely to be affected by exposure

² Many policymakers are also concerned about social effects of litigation other than economic effects, such as the extent and fairness of compensation for injuries. Thus, economic effects are an important consideration, but not necessarily the only one, for policy design.

³ Less extensive information is also presented about other mass torts since 1990 that have been very costly to drug companies, namely, Avandia, Bextra, and Seroquel.

to these kinds of liability and, if so, the kinds of company decisions that are most likely to be affected.

Chapter Seven offers summary and concluding remarks addressing, for example, major legal developments since 1990, major liability-based incentives alternatively tending to undermine or promote economic efficiency, differences in the federal preemption status among categories of medical products, and high-priority issues for further analysis.

Conceptual Framework for the Analyses

This study analyzes economic effects of several kinds of litigation involving prescription pharmaceuticals. Let's define the *liability exposure* of a manufacturer associated with a particular (existing or potential) drug as comprising the probabilities and company costs associated with legal claims concerning this drug. The two major direct costs associated with liability¹ are (1) the defendant company's payments resulting from settlements and trial judgments,² which I refer to as *indemnity payments*, and (2) expenditures on legal defense.^{3,4}

This monograph contains two kinds of analyses, namely, positive (or descriptive) and normative (or prescriptive) analyses. The positive analyses pertain to actual or potential economic effects of liability exposure, but not the social desirability of these effects. In contrast, normative analyses address social desirability. The normative criterion used here is economic efficiency.⁵

As detailed below, the basic approach used in this monograph to consider economic effects of pharmaceutical liability is to (1) develop empirical information about potential company liability costs associated with different types of litigation, (2) draw inferences about likely company responses based on well-established conceptual perspectives on decisionmaking, (3) consider the likely efficiency consequences of those responses, (4) identify particular aspects of the legal environment that create or strengthen incentives for companies to make socially desirable

¹ For some drugs, there may also be several important indirect liability costs, such as decreased demand for (sales of) a drug that is the subject of litigation because, for example, physicians hesitate to prescribe it, patients hesitate to use it when prescribed, or both. Other potential indirect liability costs include damage to a company's reputation that could reduce sales of drugs other than the one involved in litigation, costs of complying with Corporate Integrity Agreements that result from litigation, and higher insurance premiums (if the company carries insurance). Moreover, in principle, liability costs could affect decisions and economic outcomes by reducing cash on hand to fund research and development efforts.

² Within a mass tort that results in large indemnity payments, the aggregate costs of settlements are typically much larger than are the aggregate costs of claims that result in trials.

³ Pharmaceutical companies are typically not insured for costs of legal defense or for most indemnity payments associated with product-liability actions. For example, Merck & Co. (2011, p. 124) states that the company "has no insurance for certain product liabilities effective August 1, 2004, including liability for . . . products first sold after that date." At least some drug companies do, however, buy "excess" insurance to cover indemnity costs above a fairly large amount (such as \$25 million) in particular cases. Thus, effects of defendants being insured for parts of their liability costs are not considered in the analyses that follow. It appears, however, that many companies do carry directors' and officers' insurance to cover SCA claims (see Chapter Six) and shareholder derivative actions.

⁴ In addition to payments to outside counsel, there are defense costs associated with time spent working on litigation by law department and other staff of a defendant firm.

⁵ Considering only economic efficiency as a normative criterion does not address other concerns of policymakers, such as distributional issues, particularly the fairness of compensation.

and socially undesirable decisions,⁶ and (5) seek ways to strengthen incentives that encourage desirable behavior and to weaken incentives that encourage undesirable behavior.

Positive Analysis: Effects of Liability Exposure on Company Decisions and Economic Outcomes

For the positive analyses in this study, the emphasis is on drug company liability costs and how those companies' decisions are likely to be affected by liability exposure. Little attention is paid to plaintiff-side costs in this context because the economic outcomes of interest result primarily from decisions made by drug companies, and it is companies' potential liability costs that drive these decisions. Most fundamentally, changes in liability exposure associated with particular prescription drugs or prescription drugs generally—due, for example, to changes in law—alter the financial incentives of manufacturers when they make decisions.

Our interest centers on how potential changes in liability policy would be likely to affect economic efficiency. Thus, the company decisions of interest for our purposes are future decisions, not past ones. Moreover, it is emphasized that in making decisions in response to liability exposure, company decisionmakers should—and are assumed to—consider future liability environments, not historical ones. This is because the liability consequences of decisions made in the present occur later—and possibly several years later. In sum, historical liability costs associated with past company decisions—which are considered in detail in subsequent chapters—are relevant to the extent that they help company decisionmakers anticipate the nature of the future liability environments that will determine the eventual liability consequences of company decisions that have yet to be made.

Figure 2.1 depicts the conceptual framework for positive analysis. Economic outcomes prominent in the policy debate are listed on the right-hand side of the figure, which emphasizes product safety and effectiveness, the outcomes of central concern in this study. All of the indicated outcomes result primarily from company decisions, which themselves respond to incentives provided by market forces, FDA regulation,⁷ and the anticipated future liability environments. Mediating between incentives and economic outcomes are how company decisionmakers perceive their incentives⁸ and the goals or objectives that guide their decisions. The remainder of this section elaborates on this framework.⁹

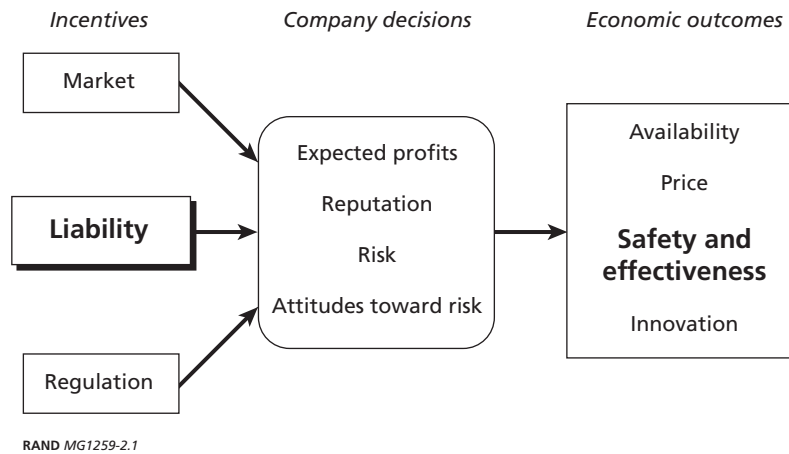
⁶ Socially desirable effects of liability exposure might include, for example, increased compliance with (most) FDA regulations and provision of more accurate information to the FDA, prescribers, and consumers. Socially undesirable effects might include, for example, provision of safety information in ways that are likely to be ineffective and withdrawing from the U.S. market a drug whose population health benefits exceed the social costs of injury.

⁷ Regulation is better viewed as an incentive than as a constraint on company choices because (FDA) regulation and enforcement do not make it impossible or infeasible for companies to take actions that conflict with regulations. Rather, pharmaceutical companies can (and, at least allegedly, often do) violate FDA regulations, and sometimes lack of compliance leads to substantial company costs. An example (see Chapter Six) is company costs associated with settling DOJ actions alleging violations of FDA regulations.

⁸ These decisions may be inaccurate because company decisionmakers do not have all of the information that bears on their future liability exposure and because—like all human beings—company decisionmakers are subject to psychological biases.

⁹ Although not indicated in the figure, liability can also affect regulation (e.g., the FDA may take action in response to information revealed in the course of litigation) or markets (e.g., prescribers and consumers may shy away from using drugs

Figure 2.1
Conceptual Framework for Inferences About Economic Outcomes



Company Decisions and Economic Outcomes

The company decisions of interest are those that substantially influence the economic outcomes of concern to policymakers. These outcomes include (1) product availability, (2) prices, (3) innovation, and (4) safety and effectiveness. Product availability pertains to whether an already developed (equivalently, existing) drug can be purchased and used by U.S. consumers, which requires that a manufacturer or other seller be willing to make it available in the United States.¹⁰

Table 2.1 lists major decisions of manufacturers that determine product availability, prices, innovation, and product safety and effectiveness.¹¹ Availability in the United States of an already developed drug requires, first, that the product be offered for sale in the United States. As will be discussed in Chapter Three, this requires that the manufacturer or seller that owns the rights to the drug in the United States obtains FDA approval. Ongoing availability on the U.S. market requires that the manufacturer continues to offer it for sale or, equivalently, not withdraw the product from the U.S. market. Drug companies influence prices paid by consumers by setting list prices and deciding what discounts to offer to large buyers, such as pharmacy benefit management companies and large health plans.¹² Innovation—the invention and commercialization of new drugs—is determined by many decisions drug companies make regarding the scientific and medical expertise of their research and development (R&D)

embroiled in litigation). Examples of these potential effects are offered in later chapters. These possibilities are not indicated (with arrows) in the figure to emphasize the central points for the present discussion.

¹⁰ The policy debate (see Chapter Five) emphasizes total lack of availability in the United States. A less extreme availability problem is shortages of products that remain on the U.S. market, which are discussed in Chapter Five in the context of some vaccines.

¹¹ Often, innovation is defined to include two phases, namely, invention and commercialization. When product availability is defined as an outcome distinct from innovation—as is the case in the liability policy debate and in this study—*innovation* really refers to the *invention* phase or, using industry jargon, *drug development*.

¹² Prices paid by consumers with insurance for drug costs are also determined by the coverage and reimbursement policies of their insurers, which are not entirely determined by drug company decisions.

Table 2.1
Economic Outcomes and Major Associated Decisions of Pharmaceutical Companies

Economic Outcome	Company Decisions
Product availability	Offering product for sale in the United States Withdrawing product from the U.S. market
Prices paid by consumers	List prices Discounts to large buyers
Innovation	Research capabilities to develop Research leads to follow Laboratory testing Conducting clinical trials
Product safety and effectiveness	Design: chemical structure or biologic agent Laboratory and clinical (human) testing Medical conditions targeted (“indications” for which to seek FDA approval) Recommended dosage levels Labeling (warnings, etc.) Information reported to the FDA Promoting products to prescribers and consumers

staff, what potential drugs (molecules or biological agents) seem promising enough upon initial screening to follow up with additional efforts, what laboratory (including animal) testing to conduct, which drug candidates will undergo clinical (human) trials, and the details of those trials.

The analyses in this study emphasize product safety and effectiveness,¹³ which can be thought of as comprising the number and severity of drug-related injuries and the number of people whose health improves to different degrees from using the drug. These outcomes depend on several kinds of company decisions. One major factor determining these outcomes depends in part on the design or physical properties of a drug, which are defined by the chemical structure (specific molecule) of the active ingredient or the biological agent.¹⁴ The chosen design (and its safety and effectiveness) depends on the testing the company undertakes to assess effectiveness and potential injuries (side effects) or risks.

Once a drug is designed and approved for sale by the FDA, the company can affect the safety and/or effectiveness of a drug by influencing who takes it¹⁵ and how they use the drug.¹⁶ Who takes the drug and how they take it can be influenced by several company decisions listed in Table 2.1.

First, as will be described in Chapter Three, drugs are approved for sale by the FDA to treat only specified medical conditions or *indications*. These approved indications have major

¹³ Other economic outcomes of policy concern are, however, discussed in Chapter Five in the context of the debate about economic effects of pharmaceutical product liability.

¹⁴ Drugs also contain inactive ingredients, such as preservatives, binders, fillers, and coatings.

¹⁵ For example, people with different medical conditions to be treated with the drug and different other medical conditions (“comorbidities”) or who are taking other drugs that might dangerously interact with the drug.

¹⁶ For example, different dosages, frequencies of use, whether they comply with their prescribers’ instructions, and how they respond to signs of dangerous side effects.

influence on who takes the drug.¹⁷ Second, how the drug is used depends on recommended dosage levels, which are proposed by the manufacturer and approved by the FDA or agreed upon based on negotiations between the FDA and the company. Third, who uses the drug and how depend on the product labeling (including warnings, contraindications, and so on), which is also proposed by the manufacturer and approved by the FDA or determined by negotiation. The product labeling at the time that a drug is first sold in the United States is often modified later (with the approval of the FDA) based on experience with the drug. Fourth, the safety and effectiveness of a drug depends on what information the company provides to the FDA either before the drug is approved or after it is marketed. For example, if a drug company does not report information about risk completely and accurately to the FDA (which would typically involve failure to comply with regulations), this failure will often undermine safety. Fifth, how many people use the drug and who uses it depend on how manufacturers promote their products to physicians and to consumers.

Almost all of the company decisions considered in this monograph apply to the entire U.S. market. In particular, few of these decisions can be made to apply or pertain to particular states or collections of states. For example, when a drug is made available in *any* state, it is made available in *all* states. Moreover, list prices are uniform across the states and newly developed drugs will be offered for sale in all states if they are offered for sale in any state. As a final example, the product labeling is, by law, uniform throughout the country. In contrast, some types of product promotion can differ across states. The extent of such geographic variation is unclear and not important for what follows.¹⁸

Conceptualizing Company Decisionmaking

Interpreting company decisions and predicting how changes in the liability environment would affect future decisions require assumptions about company decisionmaking. Such assumptions would address the company's goals or objectives, constraints on choices (such as legal rules that cannot be violated without detection), and perceptions of company decisionmakers about the likely or potential liability consequences of different decisions under consideration.

In elementary or textbook treatments, economists typically assume that business entities seek to maximize their profits, and I assume throughout that profits are, indeed, the main objective or goal of drug companies. There are at least two factors not addressed in the simplest models that are important for our purposes, however.

First, in the real world, companies care about profits in the current year (say), but they also care about profits in future years. This complication is easily dealt with conceptually, in

¹⁷ As elaborated in Chapter Three, physicians may legally use a drug to treat medical conditions other than the "approved indications," but FDA regulations prohibit drug companies from promoting their products for such "off-label" use.

¹⁸ Pharmaceutical companies promote their products to both prescribers and consumers. They promote products to prescribers in several ways, including advertising in medical journals, one-on-one meetings between company sales representatives (typically called "detailers"), and company-sponsored seminars. It is possible, at least for detailing and seminars, for drug companies to concentrate their efforts in particular geographic areas. Promotion of prescription drugs to consumers, which is called direct-to-consumer (DTC) advertising, has grown considerably since the FDA eased restrictions in 1997. DTC ads can be seen on television, in newspapers and magazines, and on the Internet and heard on the radio (Donohue, Cevasco, and Rosenthal, 2007). It is possible to concentrate such advertising in particular geographic regions, for example, by placing ads in selected newspapers, on television programs that are more popular in some areas than others, or by buying time on selected local cable outlets.

particular by assuming that companies seek to maximize the present (or discounted) value of all future profits.

Second, the consequences of many company decisions—and this is clearly the case for eventual liability costs—are uncertain when these decisions are made. Again, this complication is easily dealt with conceptually. I posit that decisionmakers use the information they have to form beliefs—summarized by subjective probability distributions—about the consequences of each potential course of action and make their decisions to maximize (mathematically) *expected* profits. More specifically, company decisionmakers form their beliefs about the eventual liability costs of different courses of action based on what they think they know—or their *perceptions*—about these consequences. Presumably, the primary basis for forming such beliefs is their interpretations of history; specifically, the liability consequences of past decisions by drug companies. Such perceptions may, however, be substantially at odds with those that would exist if the decisionmakers had substantially better information than they actually do about the liability consequences of decisions made by other drug companies.^{19,20}

What Determines Whether Companies Respond to Liability Exposure?

For the analyses reported below, a fundamental question is the conditions under which a company's decisionmakers are likely to consider ways to reduce their (perceived) liability exposure. For example, if a company perceives that a particular type of litigation threatens to cost them \$10 million over the next ten years, is that threat large enough to expect them to alter their decisions to reduce that exposure? If not, how large a threat would be required for them to consider changing decisions? From an economic perspective, the answer is that we should expect companies to consider modifying their planned behavior if and only if they believe that their savings in future liability costs (the financial benefits to the companies) would exceed the financial cost of modifying their behavior (for example, decisionmaking costs, lost sales from adding warnings).

What Kinds of Conclusions Are Possible from the Positive Analytic Approach?

As described in the introduction to this chapter, drawing conclusions about economic effects requires inference about how companies perceive their liability exposure and how these perceptions are likely to affect decisions that affect economic outcomes. The information available to support such inferences is fairly limited, however. As a consequence, it is not possible to separate the effects on company decisions of the different forms of liability that affect the same company decisions. As we will see, however, different forms of liability can affect a company's

¹⁹ Decisionmakers are likely to be well-informed about the decisions and liability experiences of their own companies but less so about the experiences of other companies.

²⁰ Robust findings in the behavioral psychology literature—key sources include Tversky and Kahneman (1974, 1981) and Slovic, Fischhoff, and Lichtenstein (1987)—suggest in the present context that decisionmakers are likely to systematically (i.e., in predictable ways) misestimate the likelihoods of some liability-cost outcomes. Most important, perhaps, is the *availability heuristic*. The availability heuristic has been succinctly explained as “people using this heuristic judge an event to be likely or frequent if instances are easy to imagine or recall” (Slovic, Fischhoff, and Lichtenstein, 1987, p. 19). Most important for our purposes, company decisionmakers may overestimate the probabilities of liability and punitive damages being assessed in legally inappropriate circumstances and exceptionally large compensatory and punitive jury awards. This is because actual or putative instances of such events appear to receive disproportionate attention in trade and mass media reports, litigation reporters, and policy advocacy documents and discussions, thus making them easy for company decisionmakers to imagine or recall.

incentives for different identifiable sets of decisions. For example, many of the relevant actions brought by the DOJ suggest future potential costs for some forms of product promotion but are reasonably assumed not to affect company decisions about drug design.

Normative Analysis: Economic Efficiency of Effects of Liability Exposure

This section discusses evaluation of economic effects in terms of their social desirability.

Economic Efficiency

For studying *economic* effects from a societal (national) standpoint, the appropriate standard for public policy evaluation is economic efficiency. Broadly stated, economic efficiency involves wisely using the limited resources available to an economy to maximize or increase the aggregate social value of what the economy produces. Stated differently, this social goal is to increase the aggregate, material-based, well-being of all residents of the United States—or the average standard of living—regardless of the distribution of well-being across members of society.²¹ As is often not appreciated, a crucial consideration in assessing economic efficiency in the context of pharmaceuticals is injuries, because injuries are crucial in determining the well-being of many U.S. residents.

This study considers the economic efficiency consequences or effects of PPL for personal injuries (see Chapters Four and Five) and related litigation (see Chapter Six). For our purposes, there are two general considerations related to economic efficiency, namely, (1) the efficiency consequences of liability-induced changes in decisions made by pharmaceutical manufacturers and consequent changes in economic outcomes and (2) the resource (or transaction) costs of disputing.

Legal disputing determines whether money will be paid by manufacturers to those who bring legal claims against them.²² A payment or transfer of money has no direct consequences for economic efficiency because efficiency pertains to the aggregate material well-being in the United States regardless of its distribution among members of society. In contrast, the resources used or absorbed in disputing—such as the time of lawyers, experts, judges, and juries—cannot be used for other purposes and, thus, do have direct efficiency consequences. In short, resources devoted to disputing legal claims involve social (opportunity) costs. Considering transaction costs is important because studies have shown that the transaction costs of disputing tort claims are considerable.²³

Thus, the overall efficiency of the forms of liability addressed in this monograph depends on the efficiency effects on company decisions—which may be socially desirable or the opposite—and the transaction costs of disputing—which must be socially undesirable.

²¹ Fairness of compensation is also a major concern of many policymakers—and this concern may play a crucial role in how policy evolves—but policy evaluation of compensation, per se, is beyond the scope of the present analysis.

²² Specifically, the legal disputes considered in this monograph are about whether money will be paid to personal-injury claimants (in the case of product liability), the federal government (DOJ claims), state governments (AG suits), private plaintiffs asserting financial injury, or shareholders.

²³ For example, Kakalik and Pace (1986) found that tort litigation (excluding auto accident cases) cost the economy about \$1.35 in resources to transfer \$1.00 to plaintiffs.

Alternative Approaches to Assessing Economic Effects

The claim that the fundamentally inferential approach applied in this monograph appears to be the most informative analytic approach is discouraging. Basing policy guidance on findings from studies using unreliable analytic approaches would be even worse. In short, it is important for policymakers to know what is not known. In this sidebar, I consider potential alternatives to the approach used in this monograph and explain why they seem unpromising for developing sufficiently reliable information for policy guidance.

While it is impossible to prove that no other empirically based analytic approach would be reliable and more informative than the approach used in this study, it seems useful to consider the feasibility alternative approaches and, if feasible, their reliability and generalizability. Consider, in turn, two major categories of alternative empirical approaches, namely, statistical analysis and case studies.^a

The first alternative general approach involves using statistics or econometrics to estimate effects, other things equal, of overall liability exposure—or particular aspects of the legal system—on economic outcomes, such as those listed in Table 2.1. For an econometric approach to be feasible, (1) it must be possible to create variables representing the economic outcome and the legal concept(s), and (2) there must be sufficient sample variation in the outcome and legal variables to enable estimation. The basic strategy of such an approach might involve exploiting variation in legal variables across the states or countries, over time, or across geographic areas and time periods.

In fact, the only arguably measurable economic outcome of direct policy interest is price.^{b,c} For example, Manning (1997) uses multiple regression analysis to consider the role of several measures of product-liability risk in the United States to analyze differences between the United States and Canada in the (logarithms of) factory list prices of 119 drugs in 1990. He concludes that product-liability risk increases drug prices in the United States.

Lack of adequate sample variation is another major challenge. Regarding variation across the U.S. states, there is little, if any, variation in outcomes. More specifically, product prices do not vary systematically across states, nor does product availability (if a drug is available anywhere in the country, it is typically available everywhere in the country), nor do innovative inputs or outputs. Most importantly for present purposes, aspects or determinants of safety and effectiveness tied to the physical properties of a drug's active ingredient(s) cannot vary across states (because the active ingredients define the drug), nor (by law) can the product labeling. There is likely to be some variation across states, however, in product promotion; but it is doubted that this variation is very substantial and, in any event, measuring promotion at the state level appears to be infeasible because of lack of data.

^a The discussion here describes selected studies aimed at understanding economic effects of pharmaceutical product liability. (There appear to be no analogous studies concerning effects of the other forms of litigation considered in Chapter Six.) I defer discussion of other studies of effects of pharmaceutical product liability to Chapter Five, because I provide essential background for that discussion in Chapters Three and Four.

^b Drug prices are not as easy to measure as some might expect. This is because, for example, in the United States different drug purchasers (e.g., retail pharmacies, pharmacy benefit management companies, and large buyers, such as health plans or hospital systems) pay different prices for the same drugs.

^c We cannot, for example, observe or measure the safety or effectiveness of particular drugs, which depend not only on their physical properties but also on who takes them and how. Moreover, the extent and mix of R&D expenditures (key inputs to innovation) cannot be observed or measured, no less the output of R&D, namely innovation.

For statistical or econometric estimates of effects of legal variables on economic outcomes to be reliable (i.e., to produce results that policymakers should trust), (1) the variables (and particularly the legal variables) must be reasonably accurately measured, and (2) the analysis must also account for other major determinants of the outcome variable that may be correlated with the legal variables.^d Accurate measurement of legal variables—for analysis across countries, for example—seems typically to be infeasible.^e

In sum, statistical approaches are typically plagued by seemingly insurmountable problems of measurement, lack of variation in outcomes and legal environments, difficulties in controlling for extra-legal determinants of outcomes, or some combination of the three.^f

Another general approach is (more or less extensive) case studies of particular drugs or classes of drugs that have been embroiled in substantial product-liability litigation. Case studies are subject to two major kinds of difficulties, namely, problems of so-called *internal* validity, which pertains to whether the conclusions or findings for the particular case are reliable, and *external* validity, which pertains to whether the findings of the study generalize to other cases.^g

As an example of potential problems with internal validity, consider Bendectin, a drug to treat morning sickness. Hundreds of personal-injury lawsuits were filed, mostly during the 1980s, alleging that Bendectin caused birth defects, despite little or no reliable scientific evidence that the drug was capable of causing such injuries (Lasagna, 1991; Green, 1996; Sanders, 1996). The product was withdrawn from the U.S. market in 1983, and many observers believe that a drug with considerable support in the medical community was driven off of the market by product liability. But Lasagna (1991), Green (1996), and Sanders (1996) do not entirely agree on the causes of the withdrawal of Bendectin from the U.S. market.^h

^d In the jargon of econometrics, these concerns pertain to estimation biases due to “errors in variables” and “omitted variables,” respectively.

^e For example, Manning (1997) uses as measures of product-liability risk in the United States (1) the number of “cases” (which ignores settlements prior to lawsuit filings) involving the drug divided by the drug’s sales, (2) the proportion of those cases won by the plaintiff, and (3) whether the prices of the drugs during the period 1977 to 1993 are sufficiently correlated with the prices of two childhood vaccines whose prices clearly seem to have been greatly affected by product-liability exposure. (See Manning, 1997, pp. 217–221, who acknowledges the problematic nature of these measures.)

^f Yet another unpromising empirical strategy is empirically analyzing effects of liability on economic outcomes for products other than pharmaceuticals. This strategy is impeded by the same problems that impede reliable study of pharmaceuticals. Moreover, it is not safe to assume that economic effects of liability in other industries are revealing about effects in pharmaceuticals because, for example, product-liability law for pharmaceuticals differs in important ways from the law for other products (see Chapter Three) as do market incentives and regulatory factors.

^g Swazey (1991, p. 291) begins her nonstatistical study with a sentence that reinforces the view that case study approaches face daunting challenges: “Assessing the effects of product liability on the safety of prescription drugs is a complex and, in some respects, ‘mission impossible’ task for many reasons.”

^h Compare Lasagna (1991, p. 340)—“Eventually, [defendant] Merrell decided to set a limit to its liability”; Sanders (1996, pp. 30–31)—“Bendectin was a casualty of the litigation” at least in part because the drug’s sales had been greatly reduced by physician and patient safety concerns that were created or heightened by the litigation; and Green (1996, Chapter 11), who considers the withdrawal in substantial detail, recounts and accepts the relevance of economic forces related to litigation, but adds the possibility that “Merrell anticipated the political benefit it might gain from making Bendectin into a victim of an expansive, extravagant tort system and overzealous attorneys, and sought to capitalize on that prospect” (p. 186).

As an example of potential problems with external validity, consider Mastroianni, Donaldson, and Kane (1990, Chapter 8), a report of the Institute of Medicine (IOM) of the National Academies, who offer case studies of the liability histories of several contraceptives (including the Dalkon Shield intrauterine device, other intrauterine devices, and oral contraceptives). They conclude “that recent products liability litigation and the impact of that litigation on the cost and availability of liability insurance have contributed significantly to the climate of disincentives for the development of contraceptive products” (p. 141). Assuming that this conclusion is correct, the external validity issue is whether these conclusions pertain to pharmaceuticals other than contraceptives. Reasons to be concerned about external validity in this context include the differences between contraceptives (for which many products compete in the marketplace) and other drugs whose profitability is considerably higher because of lack of competition.

In sum, case study approaches are often subject to reasonable doubts about internal validity and seemingly insurmountable problems of external validity.

Identifying Sources of Inefficiency

When searching for reforms in pharmaceutical liability policy or evaluating proposed reforms, a key issue for policymakers is how could efficiency be enhanced? The most promising analytic approach to answering that question is to consider several questions pertaining to transaction costs and behavioral effects of liability. One question is how might transaction costs of litigation be reduced? Other central questions are (1) what aspects of liability-based incentives are most advantageous in terms of promoting socially desirable decisions? (2) what aspects of incentives are most problematic in terms of encouraging socially undesirable behavior? and (3) how can the liability system—and, thereby, incentives—be changed to preserve the socially beneficial effects of liability while at the same time ameliorating its socially detrimental effects?²⁴

²⁴ Using this basic approach, Garber (1993) concluded that the economic effects of product liability for prescription pharmaceuticals had been a mixture of socially desirable and socially undesirable effects. He concluded that efficiency could be enhanced by improving procedures for weighing scientific evidence about injury causation, making compliance with FDA regulations a safe harbor against liability while preserving (substantial) noncompliance as grounds for liability, and clarifying standards for the availability of punitive damages.

The Legal and Institutional Settings

This chapter provides background about regulation and litigation involving prescription drugs that is required for the discussions and analyses contained in subsequent chapters.¹ First, I review pertinent aspects of pharmaceutical regulation by the FDA, emphasizing the distinction between regulations that apply to a drug that has not yet been approved for sale in the United States and regulations that apply after a drug has been introduced to the U.S. market. The following section reviews the basics of product-liability law pertaining to personal injuries allegedly caused by use of prescription drugs, which differs in important ways from legal doctrine that applies to most other products. I then discuss several other legal issues and practices that apply to prescription drugs (and more broadly).

Food and Drug Administration Regulation

The FDA regulates many aspects of drug-company behavior relating to prescription pharmaceuticals. The FDA's responsibilities and powers are specified in the FDCA. This section provides an overview of those aspects of FDA regulations relevant to the discussions and analyses contained in the following chapters.

FDA regulations pertaining to a particular prescription drug apply to the time period before that drug is approved for sale in the United States (*preapproval* or *premarket* period), after it is approved (*post-marketing*), or both. The main contours of preapproval regulation have been in force for several years and are discussed in Blanchard (2001) and Baciú, Stratton, and Burke (2007)—the latter is a report of IOM. Hyman, Phelps, and McNamara (2007) and Kessler and Vladeck (2008) summarize provisions of the Food and Drug Administration Amendments Act (FDAAA) of 2007.² I consider preapproval and post-market regulation in turn.

Preapproval Regulations

To sell a new prescription drug³ in the United States, the drug must be approved for sale by the FDA for one or more “indications” or medical conditions. To receive approval to market a new

¹ Background pertaining only to the safety- and effectiveness-related litigation discussed in Chapter Six is deferred to that chapter.

² The FDAAA of 2007 provisions of substantial importance for our purposes are contained in Title IX of the act, which pertain to post-market regulation.

³ The regulations described here pertain to drugs that have not previously been sold in the United States. Considerably less extensive regulations apply to a generic drug—an unbranded drug containing the same active ingredient as a branded drug that enters the market after the patent(s) on the branded drug expires. Most importantly, generic drugs, which may have

prescription drug for a particular indication, its manufacturer (more generally, its “sponsor”) must submit sufficient information—including results of laboratory tests and clinical (human) trials—to convince the agency that the drug is (sufficiently) safe and effective for treating that indication at the dosage levels to be recommended to prescribers. In many cases, FDA approval is granted only with the understanding that the manufacturer will conduct further (“phase 4”) clinical trials after the drug is marketed. A drug is defined by its physical properties or the drug’s “design.” If a manufacturer alters the active ingredient(s) then, by law, it is a different drug, and to be legally sold in the United States, the new drug must start at the beginning of the process required for FDA approval.

Preapproval regulations of substantial interest for the purpose of this monograph pertain to manufacturing and labeling as well as design. Manufacturing facilities and practices are also regulated before (and after) approval. Before a drug can be sold in the United States, the FDA and sponsor must agree on the product labeling, which, most importantly for our purposes, includes risk or safety information, such as warnings about side effects, contraindications, drug-to-drug interactions, and approved indications for use. The labeling of a drug is, by law, uniform across the states.

Post-Market Regulations

Product labeling continues to be regulated by the FDA as long as a drug remains available for sale in the United States. As discussed in Baciu, Stratton, and Burke (2007, pp. 37–39), knowledge about a drug’s risks is far from complete at the time a drug is approved. Such knowledge is likely to be especially incomplete regarding risks of long-term use and side effects that are relatively rare, as well as risks and effectiveness for members of demographic groups not represented in clinical studies and for people with indications that the sponsor did not study or for which the drug is not approved.⁴ In order to inform FDA consideration of changes in labeling, for example, companies are required to report to the FDA “adverse events” (AEs)⁵ experienced by people who take their drugs.⁶ AE reporting is viewed as an important safeguard, because AEs might be indicative of unknown risks or higher than expected rates or severity of side effects that should be reflected in product labeling.

Partly as a result of recognition of this lack of knowledge, the FDA can, with new powers provided by the FDAAA of 2007, require sponsors to conduct additional studies after a drug is first marketed in the United States and require them to make labeling changes if the agency and the sponsor cannot agree on what changes are appropriate. Updating warnings—for example, including previously unreported risks or higher than expected incidence of previously listed

different inactive ingredients than their branded counterparts, do not have to go through extensive testing to be approved by the FDA for U.S. marketing. Instead their sponsors must demonstrate to the FDA bioequivalence of the generic drugs to those of the corresponding branded drugs (that did go through extensive testing). Moreover, generic drug manufacturers must also show that their production facilities meet the FDA’s requirements (Frank, 2007).

⁴ While studying a drug more extensively before approval could add to this knowledge, doing so would add “considerably to the time and expense of drug approvals, which would delay patient access to potentially beneficial drugs” (Baciu, Stratton, and Burke, 2007, p. 38).

⁵ It is widely acknowledged that many AEs that are reportable under the law go unreported (see Baciu, Stratton, and Burke, 2007, pp. 55, 109).

⁶ More specifically, companies are required to report within 15 days severe AEs and side effects that are not included in the current labeling. They are also required to report all AEs quarterly for the first three years a drug is on the U.S. market and annually thereafter (Baciu, Stratton, and Burke, 2007, p. 53).

side effects—is appropriate from a public-health standpoint as additional information becomes available. Sources of such additional information include, for example, additional studies performed by the sponsor, other studies, and AE reports.

The FDA also regulates product promotion. Most importantly for what follows, physicians may legally prescribe drugs for off-label (unapproved) uses and often do so.⁷ Most forms of promotion by pharmaceutical companies for off-label uses are illegal, however; even if the provided information is accurate (U.S. Government Accountability Office, 2008; Stafford, 2008; Mello, Studdert, and Brennan, 2009). Mello, Studdert, and Brennan (2009, pp. 1557–1561) review the evolution of FDA regulations pertaining to off-label promotion.

The major purpose of restricting off-label promotion, which may or may not be attained, appears to be improving the information available to prescribers. There seem to be two separate goals in this regard. First, since restrictions on off-label promotion are expected to limit sales of drugs for unapproved indications, restrictions on promotion make it more likely that drug companies will conduct additional clinical trials of sufficient size and quality to gain FDA approval for additional uses. Second, there is widespread concern that in the absence of such high-quality studies and FDA approvals, studies of off-label safety and/or effectiveness reported in medical journals may be unreliable, because of small samples, poor methods, or influence by drug companies (Stafford, 2008; Pstay and Ray, 2008; Mello, Studdert, and Brennan, 2009).

Finally, it is important to note that compliance with FDA rules is far from complete, and a major reason is that the FDA has inadequate resources to effectively investigate, sanction, and thereby deter all compliance failures. (See, for example, Kessler and Vladeck, 2008, pp. 483–491.) Some violations are fairly easy for the FDA to detect—for example, marketing a drug without approval, using unapproved product labels, or promoting drugs for off-label use in print or broadcast advertisements—and, as a result, we should expect that such violations are rare. In contrast, some violations are fairly difficult to detect—such as failure to report all required information to the FDA and oral communications intended to promote off-label use—and there is considerable evidence that such violations do occur. In fact, allegations of failure to report to the FDA can be prominent in some personal-injury lawsuits, and, as described in Chapter Six, patterns of off-label promotion are commonly alleged in litigation brought by the DOJ and state AGs.

Product-Liability Law for Prescription Drugs

With a few exceptions, product liability comprises state common law and statutes.⁸ The only exception relevant to pharmaceuticals is provisions of the (federal) NCVIA of 1986, which is described in some detail in Chapter Four. Product-liability doctrine for prescription pharma-

⁷ For example, Radley, Finkelstein, and Stafford (2006) analyzed data on prescription drug use and patient diagnoses from about 725 million patient-physician encounters for 160 drugs. The 160 drugs included the 100 drugs most often involved in these encounters plus 40 randomly selected other drugs from the next 400 drugs most often involved. They found, for example, that drugs were being used off-label 21 percent of the time, and among those uses, 73 percent lacked “strong scientific support” regarding efficacy of the drug for the actual use (diagnosis).

⁸ Concerns about socially undesirable effects of product liability have, however, led the U.S. Congress to pass narrowly targeted legislation reducing in different ways seller liability for vaccines (National Childhood Vaccine Injury Act [NCVIA] of 1986), small aircraft (General Aviation Revitalization Act of 1994), materials used in implantable medical devices (Bio-

ceuticals shares many features with doctrine that applies to most other products; there are, however, some major differences that are crucial for our purposes.⁹ The laws in different states differ in several ways that are not crucial for the purposes of this monograph.

Product-liability claims against pharmaceutical manufacturers may be brought in both state and (under certain conditions) federal courts. A civil claim in a state court is typically adjudicated under the law and using the civil procedures of that state. Product-liability claims brought in or transferred to a federal court are adjudicated using state law, but federal procedures are used.¹⁰

Product-liability law specifies three broad categories of product “defects” that can subject manufacturers¹¹ to liability for compensating injuries caused by their products. The three categories of defects are as follows.¹²

Manufacturing Defects

First, manufacturers are legally liable for manufacturing defects, which exist when the specific unit(s) of a product that allegedly injured a plaintiff did not meet the manufacturer’s own specifications or design. Examples of manufacturing defects include an automobile with a steering column that was improperly assembled or a contaminated prescription drug. Liability for manufacturing defects is widely described as being *strict*, meaning that defendants are liable for injuries no matter how careful they were to avoid manufacturing defects (or how extensive their quality-control methods). Manufacturing defects in prescription drugs are fairly unusual, although there were several instances during the late 2000s, for example.¹³

Design Defects

Manufacturers can also be held liable for design defects. In this case, manufacturers are liable if the foreseeable injury risks involved in the product (as designed) could have been avoided by using a “a reasonable alternative design” (ALI, 1998, p. 14).¹⁴ Design defect cases are also fairly

materials Access Assurance Act of 1998), and antiterrorist technologies (Support Antiterrorism by Fostering Effective Technologies Act of 2002).

⁹ Most importantly, in terms of liability stemming from product design (which is relatively unimportant for pharmaceuticals) and the duty to warn (see discussion of the learned intermediary doctrine below).

¹⁰ In some instances, which state’s law should be applied is not obvious. When this is the case, it is said that there is a “choice of law” issue to be resolved.

¹¹ Entities in the chain of product distribution other than manufacturers—such as wholesalers, distributors, and retailers—can be subjected to product liability (American Law Institute [ALI], 1998, p. 15). The discussion here focuses on manufacturers because effects on manufacturer behavior are a central issue in this study.

¹² See, for example, ALI (1998, p. 14). ALI is a prestigious membership organization of judges, practicing attorneys, and law professors. ALI restatements summarize the state of the law and how it is changing in addition to suggesting how the law might best evolve in the future, and many ALI restatements have had substantial influence on judicial rulings.

¹³ Examples include contaminated batches of heparin (a blood thinner) manufactured in China and sold in the United States (Wilde Mathews and Burton, 2008); potentially leaking fentanyl pain patches (Feeley and Lopatto, 2008); a contaminated childhood vaccine (Corbett Dooren, 2007); and contaminated intravenous antibiotics and an anti-nausea drug manufactured in India (Reuters, 2010).

¹⁴ A possibly more helpful general description of a design defect is offered by Polinsky and Shavell (2010, p. 1453): “Under the design defect doctrine, a firm can be held liable for accidents caused by its product if the design of the product was defective, meaning, essentially, that a different design could have been employed that was safer and not excessively costly” [fn. omitted].

rare for prescription pharmaceuticals, in large measure because of the widespread influence on judges of comment k in ALI (1965) that emphasizes prescription drugs as the leading examples of “unavoidably unsafe products” for which manufacturers are not to be held liable on grounds of defective designs.¹⁵

Warnings Defects

The third type of product defect that can subject a manufacturer to liability is a warning defect. And, in fact, “[f]ailure to instruct or warn is the major basis of [product] liability for manufacturers of prescription drugs” (ALI, 1998, p. 14). A warning defect exists when the manufacturer could have, but failed to, provide instructions or warnings about a foreseeable risk when such a warning would have lessened or eliminated the risk (ALI, 1998, p. 14). Sellers are liable for failing to warn about risks that they knew or should have known about (ALI, 1998, p. 34). In the context of prescription drugs and medical devices, the law is unusual; specifically, according to the *learned intermediary* doctrine or rule, the manufacturer’s duty to warn is to the prescribing physician or health care professional, not to the consumer or patient.^{16,17}

Regulatory Compliance Defenses (RCDs)

It is often argued that pharmaceutical manufacturers should be protected from liability if they have complied with FDA regulations.¹⁸ The laws of some states do afford pharmaceutical manufacturers with more protection from product-liability actions if the manufacturer has complied with relevant FDA regulations—thus providing “regulatory compliance defenses” of various kinds. Regarding case law, Schwartz and Goldberg (2005, p. 175), citing Green (1997) and Noah (2000), write “several state high courts, such as those of California, Washington and Utah, have adopted, as a practical matter, a regulatory compliance defense for prescription drugs.” Regarding statutory law, Rosen (2004, fn. 2) reports that seven states have enacted stat-

¹⁵ ALI (1998) included a novel, and controversial, recommendation pertaining to the legal standard for finding a design defect in a prescription medical product. In particular, section 6(c) of the restatement reads:

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 (ALI, 1998, p. 145).

It appears, however, that that this provision has had little effect on the law. Conk (2007) refers to the restatement’s “uneven and even modest reception” (p. 800), reports that “a substantial debate ensued regarding the drug and medical devices provisions, which courts have not embraced” (p. 838, fns. omitted), and describes how the drugs and devices provisions of section 6 have been treated by courts in various states (pp. 840–843).

¹⁶ As of 2009, forty-four states had adopted some form of the learned intermediary doctrine; only West Virginia had explicitly declined to do so (Schwartz et al., 2009, p. 6, fn. 121). The basic rationale for the doctrine is that it is the prescriber, not the patient, who decides whether a prescription will be written, and thus warnings need to be communicated to the prescriber (ALI, 1998, pp. 145–149).

¹⁷ Some states have adopted exceptions to the learned intermediary rule and require (to avoid liability) adequate warnings to be given directly to the patient or consumer. Vaccines administered without an individualized weighing of risks and benefits (and, thus, no learned intermediary is involved) are the most common exception, and many states also except birth control pills (Schwartz et al., 2009, pp. 357–360; Hall, 2004, pp. 205–210). In recent years, several legal scholars have considered whether there should be another exception for pharmaceuticals that are directly marketed to patients (through DTC advertising); see, for example, Karns (2000); Mello, Rosenthal, and Neumann (2003); Twerski (2005); and Schwartz et al. (2009).

¹⁸ A common argument for such a defense is that the FDA extensively regulates prescription drugs and is more capable than judges and juries of striking a socially appropriate balance of risks and benefits.

utes protecting pharmaceutical products—to various degrees—from product liability based on compliance with FDA regulations. More specifically, Michigan’s statute provides a complete defense against liability; see also Miller (2009). Statutes in other states create rebuttable presumptions against liability (New Jersey, Colorado) or provide a defense against only punitive damages (Arizona, Ohio, Oregon, Utah).¹⁹ Analyses considering pros and cons of RCDs in the context of pharmaceuticals include Garber (1993), Green (1997), Viscusi et al. (1994), Rabin (2000), Noah (2000), Rosen (2004), and Sharkey (2008).^{20,21}

Other Legal Issues and Practices

Some of the laws and processes that shape PPL and related litigation apply more broadly than to pharmaceuticals, and little pharmaceutical-specific information is available. The remainder of this chapter provides background on these issues.

Personal-Injury Causation

According to legal doctrine, for a product seller to be held liable, the plaintiff must prove (by the preponderance of the evidence) that the injury suffered by the plaintiff was indeed caused by the product. In the context of pharmaceutical personal-injury cases, the causation issue can be difficult to resolve. One reason is that many injuries leading to personal-injury claims—heart attacks and strokes, for example—have known causes other than exposure to a particular pharmaceutical.²² Another reason is that there has been inadequate scientific study of the actual side effects of the drug at issue to inform the legal questions that arise.²³

Determination of injury causation for legal purposes raises two distinct questions. The first is known as the question of *general* causation (some authors use the term *generic* causation). The question here is, *can* the drug in question cause the injuries alleged by the plaintiff?

¹⁹ Sharkey (2007a, pp. 1022–1024) summarizes the situation as follows: “a strong super-majority of state jurisdictions stands opposed to the regulatory compliance defense; the conventional view is that regulatory compliance is simply one factor to be taken into account in tort actions.” This conventional view pertains to product-liability litigation broadly, as summarized in ALI (1998, p. 120): “a product’s compliance with an applicable product safety statute or administrative regulation is properly considered in determining whether the product is defective with respect to the risks sought to be reduced by the statute or regulation, but such compliance does not preclude as a matter of law a finding of product defect.” Gibbs and Mackler (1987) report that evidence of failure to comply with FDA regulations is often very damaging to defendants, and they describe failure to comply as a “strong sword” for plaintiffs and compliance as a “weak shield” for defendants.

²⁰ Garber (1993) concluded that an RCD would tend to promote economic efficiency by strengthening incentives to comply with FDA regulations; he acknowledged, however, that policymakers are also concerned about compensation. Viscusi et al. (1994) concluded that RCDs for pharmaceutical manufacturers should be enacted, addressing the compensation issue in their final sentence: “Litigation has proven too expensive a mechanism to compensate injuries unless deterrence of irresponsible conduct is simultaneously being achieved” (p. 1480).

²¹ Whether legal scholars, policy analysts, or commentators support or oppose an RCD seems to depend in large measure on how well they think the FDA performs its mission, how concerned they are about socially detrimental effects of tort in action, and their views on the appropriateness and effectiveness of tort as a compensation mechanism.

²² Situations in which there is only one (even suspected) cause of a particular injury—in which case the injury is often called a “signature disease” for the one cause—are fairly rare. A well-known example is a signature disease of asbestos exposure, namely, mesothelioma.

²³ As reported in the review of FDA regulations, all prescription drugs on the U.S. market have been studied in clinical trials, but such studies do not nearly resolve all uncertainty about the existence and rates of particular side effects.

If a plaintiff clears this hurdle, to maintain the viability of the claim, a plaintiff must also prevail on the question of *specific* causation, did the drug at issue cause the injury for that plaintiff?

Class Actions Alleging Personal Injuries

Product-liability litigation involving a particular drug often comprises many similar claims alleging personal injury from use of that drug. In such circumstances, combining similar claims in some fashion might substantially reduce the transaction costs of the litigation. One mechanism for combining claims is a class action, in which large numbers of claims are aggregated into a single lawsuit. To proceed as a class action, however, the courts must “certify” the class. Rule 23 of the *Federal Rules of Civil Procedure* provides general guidelines for certification of a class action in the federal courts.²⁴ Rule 23(a) sets forth four general criteria, all of which must be met for a class to be certified. For our purposes, the most important one is that there are issues of fact, law, or both that pertain to all members of the class (“commonality”).²⁵ Commonality is further addressed by Rule 23(b), which requires (among other things) that common issues must predominate.

States have their own rules for class certification, and they differ considerably across states (Watkins, 2010, pp. 291–294). The importance of states’ class certification rules may have been considerably reduced by the passage of the federal Class Action Fairness Act of 2005, which expanded the conditions under which class actions filed in state courts could be removed to federal courts.

Class actions seeking compensation for personal injuries are rarely, if ever, viable in the federal or state courts, largely because the facts involved in personal injuries tend to differ across claimants alleging personal injury from use of a particular drug.²⁶ Zimmerman (2006, pp. 16-3 to 16-4) summarized the situation as follows: “Recent decisions make drug and device mass torts for personal injury virtually impossible to certify and affirm on appeal.”²⁷

Class Actions Alleging Financial Injuries

While class actions for personal-injury claims are rarely viable, class actions alleging financial injury are often viable. Such class actions are important in the context of two of the types of “related litigation” discussed in Chapter Six, namely, CPA and similar suits brought by private plaintiffs and SCAs.

Judicial Gatekeeping of Expert Evidence

Deciding for legal purposes whether—as alleged by a plaintiff—an injury suffered by a civil claimant was caused by use of a particular drug is difficult and engenders much controversy.

²⁴ See, for example Rheingold (2006, Chapter 2, secs. III, IV).

²⁵ The other three criteria under Rule 23(a) are that (1) there are so many claims that it is impractical to deal with them individually or as sets of claims small enough to be joined (*numerosity*), (2) the named or representative plaintiffs’ claims are typical of those of the class (*typicality*), and (3) the class representative will protect the interests of all class members (*adequacy*).

²⁶ There are many other kinds of class actions that do not involve personal injuries (Zimmerman, 2006, Chapter 16, sec. II; Rheingold, 2006, Chapter 2), and many of them may be viable. Examples discussed below are class actions alleging financial injury and class actions seeking payment for medical monitoring.

²⁷ Such claims are often brought, however; Zimmerman (2006, p. 16-9) reports that one reason is that filing a class action can benefit plaintiffs by *tolling* (stopping the clock regarding) a statute of limitation (time limit on filing) for similar claims.

A central legal issue in this regard is how judges should decide whether to allow a jury to hear causation-related testimony by an expert witness. In 1993, the U.S. Supreme Court delivered a landmark ruling on this issue in the case of *Daubert v. Merrell Dow Pharmaceuticals*, a case involving Bendectin (a prescription drug discussed in Chapter Two). The main thrust of the decision was specification of criteria that federal trial (district court) judges—as “gatekeepers”—should consider to decide whether expert evidence is sufficiently reliable to be admitted. The *Daubert* decision is binding only in federal courts; many states, however, have adopted the *Daubert* criteria (Bernstein and Jackson, 2004; Cheng and Yoon, 2005).

The so-called “*Daubert* criteria” specified by the U.S. Supreme Court are multifaceted; the details are not important for the purposes of this study. For those purposes there are two key points. First, since the *Daubert* decision, for all civil cases combined, federal judges are more actively screening expert evidence (Dixon and Gill, 2001, 2002).²⁸ As emphasized by Cheng and Yoon (2005), however, much tort litigation takes place in state courts. Their empirical analysis—which exploits the fact that only some states have adopted the *Daubert* criteria—suggests that, in practice, there is essentially no difference in stringency of gatekeeping between the *Daubert* criteria and the *Frye* criteria that were used by many federal judges pre-*Daubert* and are still used in many states.²⁹ Second, defendants often petition for summary judgment on the grounds that none of the plaintiffs’ evidence bearing on injury causation—which typically is composed of expert opinions—is admissible. These petitions often lead judges to conduct “*Daubert* hearings” to determine whether plaintiffs could prevail on causation based on whatever expert testimony is admissible.³⁰

U.S. Supreme Court Decisions on Sizes of Punitive Damages

Since the mid-1990s, the U.S. Supreme Court has decided three cases involving standards for excessiveness of punitive damages awards, viewing the issue as one of “substantive due process” under the U.S. Constitution.³¹ These cases address the permissible sizes of punitive awards—in large measure in terms of acceptable ratios of punitive to compensatory awards.

The cases do not, however, address two other important issues, namely, the standards for availability of punitive damages and the fact that defendants can be repeatedly subjected to punitive damages for the same conduct in separate lawsuits. Regarding the first issue, Garber (1993, pp. 43–44, 196–197; 1998, p. 257) argued that the vagueness of standards of availability of punitive damages in many states—using terms such as “outrageous,” “oppressive,” “malicious,” “wanton,” and “gross negligence”³²—can leave corporate decisionmakers with great uncertainty

²⁸ Dixon and Gill did not, however, investigate whether this more active screening was leading to better outcomes, such as more frequent exclusion of unreliable evidence or more frequent admission of reliable evidence.

²⁹ The *Frye* rule directs judges to focus on whether the expert evidence is based on information and methods that are generally accepted in the relevant scientific community.

³⁰ Zimmerman (2006, secs. 15:181–15:192) provides an extensive discussion of issues related to how scientific evidence is treated in drug and device litigation. Rheingold (2006, secs. 6.3–6.8) discusses “*Daubert* proceedings” and how courts have handled general or generic causation questions in particular mass torts, including the prescription drugs Rezulin and Bendectin.

³¹ The three cases are *BMW v. Gore* (1996), *State Farm v. Campbell* (2003), and *Philip Morris USA v. Williams* (2007). These decisions and the controversies surrounding them are discussed by Sharkey (2009), who refers to them as the “Court’s constitutional excessiveness trio” (p. 27).

³² See ALI (1991, pp. 243–244).

about what behavior is required on their part to avoid punitive damages.³³ Regarding the second issue, the possibility of multiple punitive awards for the same behavior makes the potential size of total punitive damages extremely large and suggests that the possibility of punitive damages could have substantial effects on company decisions, especially in the context of mass litigation, thus increasing the likelihood that potential punitive damages affect corporate decisions.

There appear to be no empirical studies of how the frequency and size of punitive damages awards in PPL cases have or have not changed in response to the recent U.S. Supreme Court decisions. As the case histories of pharmaceutical mass torts during the 1990s and 2000s presented in Chapter Four illustrate, however, punitive damages awards have not disappeared and have loomed large in some mass torts. Thus, it seems safe to presume that potential punitive damages awards remain important considerations when pharmaceutical manufacturers make decisions of central interest in the present study.

Medical Monitoring Claims

Several mass torts involving prescription pharmaceuticals described below involved attempts by plaintiffs to force defendants to bear the costs of “medical monitoring” (or “medical surveillance”) of people who used their drugs.³⁴ The basic idea is that if past exposure to (use of) a drug could cause a serious injury that will not be apparent for an extended period of time—that is, if at least some of the potential injuries are “latent”—then those who have been exposed might reasonably want to undergo periodic diagnostic testing for the presence of the injury before the injury becomes apparent.³⁵

Hetrick and Sgroi (2006, p. 26) write, “the law of medical monitoring in the United States is far from settled.” They elaborate as follows:

[A] minority of states have affirmatively recognized medical monitoring claims. An even smaller number have recognized medical monitoring absent a present physical injury. The majority of the individual United States have either yet to address the issue of medical monitoring or do not have well established law on the topic.

Studdert, Mello, and Brennan (2003) consider the appropriateness of medical monitoring for pharmaceutical injuries from a public health perspective. Their analysis focuses on the Fen-phen diet drugs and the oral antidiabetes medication Rezulin while also reporting that medical monitoring claims were filed in the context of the hormone-replacement therapy (HRT) drug Prempro.³⁶ They pay particular attention to criteria used by Judge Bechtel in 2000 to review and approve a medical monitoring program that was part of a class settlement in the Fen-phen

³³ Among the kinds of behavior that almost surely expose a company to punitive damages is weighing the social costs and social benefits of safety increases even though such cost-benefit balancing is required for economic efficiency. See Viscusi (2000) and Garber (2000).

³⁴ Wajert (2006) reports that such claims have been made involving “phen-fen, Vioxx, Bextra, hormone-replacement therapy, Viagra, Lipitor, OxyContin, Fosamax, Meridia, and several other drugs.”

³⁵ According to Rheingold (2006, pp. 2-57 to 2-58), even though “there is little or no scientific basis” for believing that a substance can cause latent injury or that such a condition can be prevented or ameliorated through early detection, “[i]t has become fashionable to add a cause of action for medical monitoring to every mass tort complaint.” Rheingold (2006, p. 2-57) also reports that “to make it feasible to seek recovery of any sort for medical monitoring, the almost universal method is to seek creation of a class to make the claim and administer it.”

³⁶ Personal-injury, product-liability litigation involving all three of these drugs is discussed in Chapter Four.

litigation.³⁷ They conclude (p. 892) “the Bechtel criteria reflect a good understanding of the public health benefits and limitations of monitoring.”³⁸

While the implications of pursuing the distinct social goals of public health promotion and economic efficiency differ, several of the Bechtel criteria also seem reasonably well suited to the pursuit of economic efficiency. For example, the Bechtel criteria for approving medical monitoring include reason to believe that exposure can cause latent injury, that it is possible to detect such latent injuries at a reasonable cost, and that early detection can enable effective prevention or treatment.

Congregation and Coordination of Related Lawsuits

Much of PPL litigation involves mass torts, which are large numbers (thousands, tens of thousands) of lawsuits alleging personal injury from the same drug. And it appears that the potential for mass torts along with punitive damages are the main factors underlying the very considerable liability costs and financial risks faced by drug manufacturers.

When large numbers of related lawsuits are filed in the federal courts or in the courts of particular states, the court systems do not have the resources to deal with each case on an individualized basis. Thus, the federal court system and court systems in several states have developed procedures to manage some aspects of these cases in aggregated (or “congregated”) fashion.³⁹ When different personal-injury lawsuits are congregated, they remain separate lawsuits. Most importantly, congregations of such cases are not class actions.⁴⁰

The best-known formal congregation mechanism is the federal multidistrict litigation (MDL). The beginning of the federal MDL process involves transferring related cases filed in different federal district courts to a single district court and judge to manage the cases for pre-trial purposes. Such “pretrial” purposes include managing discovery and dealing with motions that apply to many, if not all, cases within an MDL. Among such issues is general causation, and drug-safety MDLs often involve *Daubert* motions, hearings, and rulings.

It is expected that once the pretrial processes are completed, the cases that have not been dismissed or settled will be returned to the individual district courts in which they were originally filed (Olson, 1988–89; Hensler, 2001; Rheingold, 2006, Chapter 3). In some MDLs, a fairly small number (such as five or ten) of “bellwether trials” are conducted to help the litigants anticipate the likely outcomes of trials in different kinds of cases for the purpose of informing settlement negotiations and promoting settlements (Fallon, Grabill, and Wynne, 2008). Many states have similar procedures for cases filed in various courts in their states (Herrmann, Ritts, and Ray, 2005; Ostolaza and Hartmann, 2007).

³⁷ As reported by Studdert, Mello, and Brennan (2003, p. 891), these criteria are “whether (1) the disease in question progresses asymptotically following toxic exposure; (2) a diagnostic test with high sensitivity exists; (3) the exposed population has a relatively high prevalence of disease; (4) the diagnostic test therefore has a high predictive value; (5) the test is relatively low-cost; (6) medical monitoring could be integrated into standard clinical follow-up of those with [the] disease; (7) monitoring could lead to early preventive care; and (8) monitoring allows for the appropriate timing of definitive treatment.”

³⁸ Certification of *nationwide* medical monitoring classes is generally not possible (Zimmerman, 2006, p. 16-4).

³⁹ Congregating cases so they are managed by a single judge have some obvious advantages, such as avoiding duplicative discovery and conflicting legal rulings by different courts.

⁴⁰ As reported earlier in this chapter, class actions are single lawsuits representing large numbers of claimants, and personal-injury class actions are rarely viable in federal or state courts (i.e., it is virtually impossible to have such class actions certified with certification upheld on appeal).

Usually, however, lawsuits included in a mass tort are filed in both federal and state courts, and there is no formal mechanism for consolidating all cases in a single court. It is not uncommon, however, for judges in various jurisdictions to cooperate informally (Rheingold, 2006, Chapter 4).

Settlements of Mass Torts

Since the U.S. Supreme Court decisions in *Amchem Prods. Inc. v. Windsor* (1997) and *Ortiz v. Fibreboard Corp.* (1999), settlements of mass torts cannot rely on mandatory (or “no opt-out”) class actions used for settlement purposes (Hensler, 2002; Powell, 2006; Rheingold, 2006, secs. 2:12, 2:13; Nagareda, 2007, Chapter V). Succinctly stated, “The Court’s decisions in *Amchem* and *Ortiz* have foreclosed the use of mandatory class actions as peacemaking vehicles for mass torts” (Nagareda, 2007, p. 115). Lawsuits in pharmaceutical mass torts are not, however, settled one by one. Often cases are settled on an “inventory” basis, in which a plaintiffs’ law firm settles all of its cases. In addition, defendants often attempt “global” settlements that resolve (almost) all pending cases, in some instances including claims filed as class actions (Rheingold, 2007, Chapter 9; Silver and Baker, 1997; Erichson, 2005). Sometimes, settlement amounts are specified using a “grid” or “matrix,” with these amounts depending on such factors as severity of injury, age of the claimant, the presence of other risk factors for the injury, and so on.

The next chapter describes several pharmaceutical mass torts during the 1990s and 2000s and concludes with some inferences about their likely economic effects.

Pharmaceutical Mass Torts During the 1990s and 2000s

I focus on mass torts to understand the incentives of drug companies stemming from product-liability exposure. This is because mass torts are fairly common for prescription drugs, they can involve extremely high costs and financial risks for drug companies, and (as a result) potential for mass torts is likely to be the predominant product-liability concern of drug companies as they make decisions.

The previous two decades witnessed several attempts by plaintiffs' lawyers to develop mass torts involving (alleged or scientifically established) personal injuries related to prescription pharmaceuticals.¹ Some of these attempts have succeeded from the plaintiffs' point of view in the sense that they have resulted in large—for example, \$1 billion or more—indemnity payments by defendants.² Others have largely failed in this sense. Two points are emphasized in this regard. First, “failed” mass tort attempts can be very costly to plaintiffs' attorneys; for example, their litigation expenses may leave little, if any, money to compensate clients or to provide legal fees. Second, even failed mass tort attempts can be very costly to defendants because of legal defense costs, distraction of management, and so on. Thus, defendants have financial incentives to try to avoid even those mass tort attempts that eventually fail from the perspective of plaintiffs.

This chapter provides case histories of several mass tort attempts that had been largely resolved by the end of 2011 or for which at least the broad contours of the eventual resolution seemed fairly clear by that time.³ The purposes of reviewing these cases are to (1) provide perspective on the potential scales and costs to defendants of individual mass torts, (2) indicate the kinds of company behavior that can substantially affect those costs, and (3) support inferences about whether companies are likely to consider taking actions that would be expected to decrease expected, future liability costs.

¹ There are no official lists of mass tort attempts, but there are two particularly useful sources. First, when a plaintiff's law firm or a group of firms intends to file large numbers of closely related lawsuits, it appears that the group typically forms or joins a “litigation group” of the American Association for Justice (AAJ), an association of trial lawyers formerly known as the Association of Trial Lawyers of America (ATLA). Lists of the names of apparently active litigation groups can be found on the AAJ website (AAJ, 2012). Second, lists of pending federal MDLs can be found on the U.S. Judicial Panel on Multi-district Litigation website (2012).

² Portions of these gross payouts by defendants are retained by contingency-fee attorneys and to pay the attorneys' out-of-pocket expenses in pursuing their clients' claims.

³ The mass tort attempts I review may not be the only ones that satisfy this criterion, however. Specifically, potential candidates for case histories that are not discussed are those for which I was unable to collect sufficient information from public sources to develop useful descriptions.

First, I review histories of six mass torts that have resulted in payouts to plaintiffs and their lawyers of at least \$1 billion. These mass torts involve Fen-phen diet pills, Baycol, Rezulin, Vioxx, hormone replacement therapies, and Zyprexa. Next, I consider four mass tort attempts that have largely failed from the plaintiffs' point of view, namely, Norplant, autism claims against childhood vaccine manufacturers, Meridia, and Serzone.

Mass Torts Resulting in Especially Large Payouts by Defendants

Fen-Phen Diet Pills

This mass tort involves litigation alleging personal injuries caused by drugs used for weight reduction. The widely used term "Fen-phen" refers to a combination of one of two "fens" with "phen." "Phen" refers to phentermine, which was approved by the FDA in 1959 and eventually sold in the United States by several companies. The two "fens" are Pondimin (approved in 1973) and Redux (approved in 1996). The lion's share of the lawsuits were brought against American Home Products (AHP) and Wyeth (a subsequent name for AHP) and its subsidiaries (Wyeth-Ayerst Labs, A. H. Robins).⁴ AHP/Wyeth produced and marketed Pondimin and distributed Redux under license from Interneuron.⁵ At the request of the FDA, Wyeth withdrew both Pondimin and Redux from the U.S. market on September 15, 1997 (Rheingold, 2008, supp. p. 15-4; Studdert, Mello, and Brennan, 2003, p. 891). Between 1995 and 1997, an estimated 6 million people used Pondimin or Redux alone or in combination with phentermine (Studdert, Mello, and Brennan, 2003, p. 891).

Two severe side effects of Fen-phen led to litigation (Wyeth, 2008, p. 42; Rheingold, 2008, supp. p. 15-4). The first, and much more common, injury was valvular heart disease (VHD), which is usually not fatal, but in especially severe cases requires valve-replacement surgery. The second major side effect alleged in the litigation is primary pulmonary hypertension (PPH), which is often fatal. Almost all of the injuries from Pondimin and phentermine apparently involved off-label use. In particular, the drugs were not approved for use in combination, and many doctors apparently had patients using the drugs for longer than was approved by the FDA (Rheingold, 2008, supp. p. 15-3).

The plaintiffs' liability cases emphasized FTW allegations. The labels of Pondimin or Redux had not included warnings about VHD, but both drugs included warnings about PPH (Rheingold, 2008, supp. p. 15-4). Moreover, by 1999, there were also allegations of "inadequate monitoring of consumer complaints" and an ongoing federal criminal investigation into the possibility that "the company had withheld risk information in regulatory proceedings" that "raised the possibility of multiple punitive damage awards" (Nagareda, 2007, p. 137). And, in fact, two trials during 1999 involved verdicts "including big punitive damage components" (Frankel, 2005). Plaintiffs had lost no trials through 2009 (Rheingold, 2010, supp. p. 15-4).

The Fen-phen litigation eventually involved tens of thousands of lawsuits (alternatively, *cases*) against AHP/Wyeth in state and federal courts.⁶ Table 4.1, which was constructed using figures gleaned from the company's reports to the U.S. Securities and Exchange Commission

⁴ The other major defendant was Interneuron.

⁵ Wyeth had not "manufactured, distributed or sold" phentermine (Wyeth, 2008, p. 42).

⁶ There were also about 2,000 lawsuits naming Interneuron.

Table 4.1
Number of Pending Diet Pill Lawsuits Reported to the SEC by AHP/Wyeth,
1998–2000

Filing Date	Form	Time Period	Number Pending	Number Seeking Class Status
March 29, 1999	10-K	1998	2,615	70
May 14, 1999	10-Q	1999/Q1	3,167	71
Aug. 16, 1999	10-Q	1999/Q2	4,164	81
Nov. 15, 1999	10-Q	1999/Q3	7,754	107
May 15, 2000	10-Q	2000/Q1	9,871	119

SOURCE: Disclosures by Wyeth/AHP to the SEC.

(SEC), details the accumulation of lawsuits (alternatively, *claims*) through the first quarter of 2000, at which time almost 10,000 lawsuits had been filed (of which 119 were filed as class actions). In December 1997, lawsuits filed in 58 federal district courts were consolidated into MDL 1203 in the Eastern District of Pennsylvania. As of March 15, 2011, more than 20,000 cases had been transferred to the federal MDL, and 128 cases were still pending (U.S. Judicial Panel on Multidistrict Litigation, 2012, p. 10).

By early 1999, Fen-phen lawsuits filed in New York and New Jersey state courts were consolidated and assigned to a single judge in each of these states, and in Pennsylvania, Texas, and California, other forms of aggregation of state-court cases were used (Rheingold, Coren, and Weiss, 1999). McGovern (2000, pp. 1887–1889) describes how the federal cases tended to differ from the state-court cases and how state-court judges cooperated (and, in some instances, did not cooperate) with the federal MDL judge in case management and promoting settlement.

A Nationwide Class Action Settlement (NCAS), negotiated between AHP and the Plaintiffs Steering Committee in the MDL, was proposed in 1999 and was approved by the MDL judge in the fall of 2000. Rheingold (2006, sec. 9:19) provides a description of the settlement and subsequent events. The NCAS, which was amended several times, includes provisions for claimants with VHD, but not for those with relatively minor valve-leakage claims. There is a separate class in the NCAS for medical monitoring. The NCAS did not cover PPH. AHP agreed to pay up to \$3.5 billion in the original NCAS (Rheingold, 2006, p. 2-133).

Levels of compensation for VHD are based on a matrix (or *grid*), with different amounts available to members of different subclasses defined by combinations of age at diagnosis, severity of injury, and duration of Fen-phen use (Frankel, 2005; Nagareda, 2007, p. 137). The settlement provided for more than \$1.3 million per claimant at the high end and \$7,500 at the low end to compensate for heart valve damage (Frankel, 2005). Because of the possibility of latent injuries, the NCAS provided for future claimants through 2015. As described by Frankel (2005) and Nagareda (2007), the NCAS did not achieve widespread settlement at a cost to AHP/Wyeth of anywhere near the \$3.5 billion initially provided to fund the NCAS. Two main drivers of escalating costs to Wyeth were opt-outs from the NCAS and large numbers of claims of dubious validity.

Plaintiffs (alternatively, *claimants*) eligible for compensation through the NCAS could opt out at three stages and pursue their claims in the courts, with only those opting out at the first

stage allowed to claim punitive damages; roughly 50,000 claimants did opt out at this stage. Because each of these initial opt-outs represented a potential punitive damage award, Wyeth's lawyers moved quickly to settle them at a cost of "billions of dollars" (Frankel, 2005). As discussed by Nagareda (2007, pp. 136–151), the NCAS also provided for "back-end" or "downstream" opt-out rights, and the viability of the settlement was greatly undermined by as many as 60,000 back-end opt-outs (Nagareda, 2007, p. 147).

The Fen-phen litigation has cost AHP/Wyeth roughly \$20 billion. More specifically, by the end of 2005, AHP/Wyeth had paid out almost \$15.4 billion in settlement payments and legal fees and had taken accounting charges of \$21.1 billion, with the difference representing the company's estimate of the future costs of resolving the litigation.⁷

The eventual cost to Wyeth of the litigation, then, was far more than had been anticipated at the time the original NCAS was negotiated. Accounts by Frankel (2005), Rheingold (2006, sec. 9:19; 2008, sec. 15:2), and Nagareda (2007, pp. 136–151) suggest several reasons for Wyeth's inability to control its settlement costs. These reasons include the following: large numbers of initial opt-outs combined with Wyeth's willingness to make sufficiently generous offers to settle many of these claims quickly; the existence and large-scale exercise of back-end opt-out rights; the exclusion of PPH cases and cases involving relatively minor valve leaks from the NCAS combined with filings of many more such lawsuits than had been projected; and the filing of many leakage claims that were "based on exaggerated (to say the least) readings of the echo[cardiogram] tests" (Rheingold, 2006, p. 2-134).⁸ Most of the opt-out VHD claims and most of the PPH claims have been settled (Rheingold, 2008, supp. p. 15-5).

Wyeth's costly experience trying to resolve the Fen-phen litigation has become a cautionary tale for other pharmaceutical mass tort defendants; see, for example, Frankel (2006). In particular, in light of experience with the settlement of Fen-phen litigation and with other mass torts, it appears that, at least in some more-recent mass torts, drug companies have been less prone to settle claims for (1) relatively minor injuries, (2) injuries that were plausibly attributable to causes other than the drug alleged to cause them, and (3) injuries that may not be real. For example, as discussed presently, Bayer used a strategy in Baycol litigation to settle only cases in which injury causation is clear, namely, those brought by claimants with rhabdomyolysis, and contest all other claims. In addition, in negotiating a \$4.85 billion settlement in Vioxx that is discussed later in this chapter, Merck considered Baycol as a model in an effort to avoid an outcome similar to what Wyeth experienced with Fen-phen (Tesoriero, Rubenstein, and Heller, 2007).

The Phen-fen litigation also offers a cautionary tale for society and public policymakers. In particular, the litigation apparently involved substantial numbers of claims involving plaintiffs who did not suffer injuries relevant to the litigation or for whom the severity of injury was substantially exaggerated. Many commenters have rightly focused on the unethical nature of bringing such claims. It is important to realize, in addition, that there are socially undesirable *economic* consequences of dishonest claiming. In particular, the transaction costs attributable to fraudulent claims are even more troublesome from an economic point of view than those associated with honest claims. This is because transaction costs associated with honest claims

⁷ The \$21.1 billion figure was still pertinent at the end of 2008, based on Wyeth's 10-K for 2008 (the last year before Wyeth merged with Pfizer).

⁸ For detailed accounts of large numbers of dubious, and perhaps fraudulent, claims see Frankel (2005) and Lenzner and Maiello (2006).

often represent use of scarce resources to serve socially desirable purposes, such as deterrence of socially detrimental behavior or compensation for deserving victims of drug injuries. In contrast, dishonest claiming does not serve a worthy social compensation goal, but it does send a signal to drug companies that they can pay dearly for injuries that are not caused by their products. It is difficult to imagine how such a signal might be reasonably expected to induce company responses that promote economic efficiency.

Baycol

Baycol (cerivastatin) is a cholesterol-lowering drug, one of several drugs known as *statins* (HMG-CoA reductase inhibitors). The drug was marketed in the United States by the Bayer Corporation. Baycol was approved by the FDA in 1997 and was removed from the U.S. market in August 2001 (Rheingold, 2006, p. 15-28) amid concerns about side effects involving muscle damage and especially rhabdomyolysis (Rheingold, 2006, p. 15-29).

The U.S. product-liability litigation involving Baycol emphasized FTW adequately about risks of rhabdomyolysis; some suits also alleged a design defect based on the claim that rhabdomyolysis was more common among Baycol users than users of other statins. Other personal-injury claims alleged that use of Baycol caused other forms of muscle damage, acute kidney failure, and heart attacks (Rheingold, 2008, p. 15-30).

At least 14,000 product liability and other types of lawsuits (e.g., consumer fraud, predatory pricing, unjust enrichment) involving Baycol have been filed in the United States. These lawsuits include class actions claiming compensation for personal injury, medical monitoring, economic loss, and securities fraud. Baycol cases filed in federal courts were transferred through the MDL process to the District of Minnesota (MDL 1431). Many other Baycol lawsuits were filed in state courts in Pennsylvania (Bayer is headquartered in Pittsburgh), and these lawsuits were consolidated for pretrial purposes in a state court in Philadelphia (Rheingold, 2008, p. 15-31).

During 2002, Bayer began implementing a plan to settle claims brought on behalf of Baycol users who had been diagnosed with rhabdomyolysis (*Andrews Pharmaceutical Litigation Reporter [APLR]*, November 2002c, p. 3; Rheingold, 2008, p. 15-32). An unusual feature of Bayer's settlement plan, which has received considerable attention, is that Bayer did not require confidentiality about settlement terms as a condition of settlement.⁹ In 2005, Bayer reported that it had settled 3,000 cases with indemnity payments totaling more than \$1 billion. Bayer has refused to settle cases not involving rhabdomyolysis, and many of those cases were dropped by the plaintiffs (Rheingold, 2008, p. 15-32). As of February 1, 2008, about 295 Baycol lawsuits were still pending in the United States (Bayer Corporation, 2008, p. 188).

Zimmerman (2006, p. 18-30), who served as Lead Plaintiffs' Counsel in the Baycol MDL (Zimmerman, 2006, p. v), expresses concern about lack of compensation for injuries less serious than rhabdomyolysis (which may or may not have been caused by Baycol) along with considerable satisfaction that the rhabdomyolysis settlements "were fair, they were reasonable, and they were consistent across the country for similar injuries and damages." He concludes that dedication by Bayer, the MDL Plaintiffs Steering Committee, and the MDL court to the principle of fair compensation for serious injuries "resulted in a serious and complex mass tort being resolved in record time for fair value" (Zimmerman, 2006, p. 18-30).

⁹ Anderson (2012) analyzes Bayer's incentives to be transparent about its settlement offers and provides further information about Baycol and the Baycol litigation.

Rezulin

Rezulin (troglitazone) is an oral medication for type 2 (adult-onset) diabetes. It was marketed in the United States by the Parke-Davis division of Warner-Lambert from August 1997 until March 2000 when Warner-Lambert withdrew Rezulin from the U.S. market in response to an FDA request triggered by concerns about liver injuries (*APLR*, 2001; Studdert, Mello, and Brennan, 2003, p. 892; Rheingold, 2008, pp. 15-19, 15-20). Lawsuits claiming personal injury from Rezulin use focused on liver damage, which in some cases resulted in transplants or death, with allegations including FTW and delay in alerting doctors to conduct liver function tests on Rezulin patients (Rheingold, 2008, p. 15-20). Frankel (2006) reported that there were about 23,000 Rezulin claimants.

Pfizer acquired Warner-Lambert in June 2000, and in its 2001 annual report, Pfizer reported that 5,100 people had sued for personal injuries related to Rezulin in state and federal courts (Rheingold, 2009, p. 15-22). The federal cases, including several class-action filings, were consolidated and transferred through the MDL process (MDL 1348) to the Southern District of New York in June 2000 (*APLR*, 2000). In October 2002, the MDL judge denied motions to certify an injury class and a medical monitoring class (*APLR*, 2002b; Rheingold, 2009, p. 15-21). Rheingold (2009, p. 15-21) further reports that “various types of classes have been denied in various states, including New York, California, and West Virginia.” A petition to certify a medical monitoring class in West Virginia was denied by the trial judge after reviewing the Bechtel criteria (Studdert, Mello, and Brennan, 2003) but was certified on appeal by the West Virginia Supreme Court in “a rare instance where a trial court which denied a class was reversed on appeal” (Rheingold, 2006, pp. 2-147, 15-21).

Some Rezulin trials have involved large verdicts for the plaintiffs. Examples include *Sanchez v. Parke-Davis Co.*, a Texas state-court case that was settled (for a confidential amount) while the jury was considering a punitive damage award after awarding \$43 million in compensatory damages (*Andrews Drug Recall Litigation Reporter [ADRLR]*, 2002; Rheingold, 2009, p. 15-22); and *Soto v. Warner-Lambert*, another Texas case, in which a jury awarded a total of \$29 million, including \$23 million in punitive damages (Rheingold, 2009, p. 15-22). A Mississippi state-court suit (*Cunningham v. Warner-Lambert*) was settled in 2001 for an undisclosed amount that by some accounts was \$175 million (*APLR*, 2001).

In its February 2008 10-K report to the SEC, Pfizer reported a charge of \$975 million taken in 2003 to cover personal-injury claims related to Rezulin, that many Rezulin cases had been settled, and that remaining personal-injury cases were being defended “vigorously.” Pfizer also reported that financial-injury class actions related to Rezulin had failed to attain certification in California and Texas but such classes had been certified in Illinois and West Virginia and had been settled (Pfizer Inc., 2008).¹⁰

Vioxx

Vioxx (rofecoxibin) is a pain medication that was often used by arthritis sufferers. It was available for sale in the United States from Merck between 1999 through September 2004 when it

¹⁰ Another drug in the glitazone class—Avandia (rosiglitazone)—has also been subjected to substantial personal-injury litigation. GlaxoSmithKline (2011, p. 180) reported that the company had reached agreements to settle most of the pending Avandia personal-injury lawsuits “as of February, 2011.” Feeley (2011a) reported on February 7, 2011, that the company had agreed to settle about 5,500 claims for a total of more than \$250 million, but the company declined comment. Feeley (2011d) reported that as of November 8, 2011, the company was still facing roughly 20,000 Avandia lawsuits.

was withdrawn from the U.S. market amid heightened safety concerns. Vioxx was one of three COX-2 inhibitors that had been available in the United States.¹¹ About 20 million people in the United States took Vioxx while it was on the market (Tesoriero, Rubenstein, and Heller, 2007).

Side effects apparently caused by Vioxx are heart attacks and ischemic strokes, both of which can be fatal, and sudden cardiac death. The product-liability claims emphasize FTW, alleging that the warnings to physicians were inadequate in light of what Merck knew at the relevant times about cardiovascular risks from their own Vioxx studies and from published and unpublished literature (Rheingold, 2006, p. 15-35).

A federal MDL (MDL 1657) was established in February 2005,¹² and large numbers of state-court Vioxx cases were congregated in California, Texas, and New Jersey. Numerous class actions have been filed, for various purposes, including some that sought only medical monitoring or compensation for financial loss. A medical monitoring class action was certified in New Jersey in 2007 (Rheingold, 2008, sec. 2:33).

Tesoriero, Rubenstein, and Heller (2007)—from which the information in this paragraph was adapted—provides an overview of the Vioxx litigation up to the time that a \$4.85 billion settlement was announced on November 9, 2007. Early in the litigation, Merck announced that it would settle no claims and was prepared to try them all, if necessary. Judges around the country set trial schedules so that Merck would not be overwhelmed by having to participate in multiple concurrent trials (see also Nagareda, 2008, p. 3). At the time of the settlement announcement, 16 Vioxx trials had been completed, and Merck had prevailed in 11 of them, spending \$1.2 billion of the \$1.9 billion that they had reserved for defending Vioxx lawsuits.¹³ Perhaps more important, of the five of these trials that were considered “bellwethers” (i.e., appropriate test cases for valuing claims of different types under different circumstances), Merck had won four of five.

Late in 2006, Merck changed its strategy from refusing to discuss settlement to being willing to negotiate, because of the combined influences of at least four factors. First, the trial outcomes to date had lowered plaintiffs’ lawyers’ assessments of the value of various types of Vioxx claims, in large measure because prevailing on specific causation had proved difficult for plaintiffs (*Wall Street Journal Online*, 2007; Nagareda, 2008, p. 2). Second, the federal MDL judge and the three judges handling congregations of state-court cases in Texas, New Jersey, and California—which together accounted for 90 percent or more of the pending cases—communicated to the parties on both sides their hope that the litigation could be settled (Tesoriero, Rubenstein, and Heller, 2007; Nagareda, 2008, p. 3). Third, by the time of the settlement agreement, the statutes of limitations on filing new claims had expired in more than 40 states, which meant that eventual numbers of claims could be accurately projected at the time of the settlement agreement (Nagareda, 2008, p. 3). Thus, Merck—unlike Wyeth in the case of the NCAS in Fen-phen—was largely insulated from large numbers of later claims

¹¹ The other two COX-2 inhibitors are Pfizer products; namely, Bextra (valdecoxib), which was withdrawn in April 2005, and Celebrex (celecoxib), which remained on the U.S. market as of August 2011. Roughly 7,000 to 8,000 personal-injury claims were asserted against these two drugs. In October 2008, the company announced that it had settled roughly 90 percent of the personal-injury suits, most of which involved Bextra, for about \$745 million (Johnson, 2008; Koppel, 2008).

¹² Sherman (2008, pp. 2213–2216) reviews the history of the Vioxx MDL.

¹³ Summary information about Vioxx product-liability cases tried through September 30, 2007, is contained in Merck & Co., Inc. (2008, pp. 26–29).

(which, in the case of Vioxx, would have to be litigated because they would not be covered by the settlement).¹⁴ Finally, continuing to litigate would be very costly for Merck; more specifically, the company had to that point spent \$1.2 billion, and settling would save it “hundreds of millions of dollars a year in legal fees” (Tesoriero, Rubenstein, and Heller, 2007).

Wall Street Journal Online (2007) contains the text of a Merck news release describing the settlement on the day that it was announced, including the following. The settlement covered only legal residents of the United States and claimants who alleged that their heart attack or stroke occurred in the United States. To be eligible, claimants also would have to document that they had taken Vioxx for at least 30 days and suffered a heart attack or ischemic stroke while they were taking the drug or within two weeks of discontinuing use.¹⁵ Of the total \$4.85 billion available from Merck under the settlement, \$4 billion was allocated to pay heart attack claims and the remaining \$850 million for ischemic stroke claims. At the time of the settlement, it was estimated that about 45,000 to 50,000 claimants were eligible for settlement payments.¹⁶ The settlement did not involve certification of a class. Strictly speaking, the agreement did not settle any cases, because no claimants were parties to the agreement, and lawyers must have the consent of their clients to settle their cases. The agreement is a contract between Merck and law firms with prominent positions in the litigation (Nagareda, 2008, p. 4). Claimants were required to take steps to participate in the program; thus, the program requires claimants to opt in to be eligible to receive payments.

The total dollar amounts available to pay eligible claims for the two types of qualifying injuries were, then, fixed at the outset. The settlement agreement included a point system for each eligible claim, which has been described—and to this author appears to be—as having been designed to approximate “the likely relative value of the claim in the tort system” (*Description of Settlement Agreement*, undated).¹⁷ The point system is rather complicated, depending on numerous factors such as claimant age, how many pills were dispensed to the claimant, the duration of Vioxx use, injury level or severity, and whether the claimant had other risk factors for the injury suffered (such as smoking, diabetes, hypertension, and so on).¹⁸ Thus, individual claimants could not know precisely what their payments would be if they participated in the program at the time that they had to decide whether to opt into the plan.

Merck reserved the right to withdraw the settlement offer if fewer than 85 percent of eligible claimants¹⁹ agreed to participate in the settlement by registering by January 15, 2008,

¹⁴ One of Merck’s outside counsel explained that Bayer AG’s settlement strategy in Baycol was one of the models for Merck in fashioning the Vioxx settlement, in that both settlements were clear in terms of what claims defendants were willing to settle and in requiring substantial medical evidence of eligibility for compensation under the plan (Tesoriero, Rubenstein, and Heller, 2007).

¹⁵ Claimants suffering strokes “that are hemorrhagic in nature” or transient ischemic attacks are not covered by the agreement (*Wall Street Journal Online*, 2007).

¹⁶ It was also estimated that another 10,000 to 15,000 claimants were not eligible (Tesoriero, Rubenstein, and Heller, 2007).

¹⁷ This document appears to have been prepared by plaintiffs’ counsel in the Vioxx litigation.

¹⁸ The details of the point system are contained in Exhibit 3.2.1 of Merck & Co., Inc., and The Counsel Listed on the Signature Pages Hereto (2007). Copies of this document available on the Internet, however, seem not to contain the exhibits. The complete settlement agreement is, however, contained in Rheingold (2008, sec. 17:11).

¹⁹ The 85 percent requirement applied separately to three categories of claimants, namely, those experiencing a heart attack, an ischemic stroke, or sudden cardiac death.

and enrolling by March 1, 2008.²⁰ In fact, as of early March 2008 these thresholds were easily met, with 44,000 of 47,000 eligible, registered claimants having submitted at least some of the required documentation (Tesoriero, 2008). About five months later, it was reported that 48,500 of 49,960 registered eligible claimants had “submitted forms indicating their intent to take part in the settlement” (ADRLR, 2008b).

A few months after the settlement agreement, plaintiffs’ lawyers estimated that most eligible claims would result in payment ranging from \$50,000 to \$1.5 million (Tesoriero, 2008). Merck & Co. (2011, p. 125) reports that as of December 31, 2010: (1) final payments from the Settlement Program had been made for more than 99 percent of claims involving heart attacks and strokes, and (2) “approximately 35 plaintiff groups who were otherwise eligible for the Settlement Program did not participate and their claims remain pending.”

Hormone Replacement Therapies—Premarin, Provera, and Prempro

There has also been a substantial volume of litigation alleging personal injury to post-menopausal women who took one or more of several drugs—some generic and some branded—that replace the hormones estrogen, progesterone, or both (HRTs). Much, and perhaps most, of this litigation has been brought against Wyeth, Upjohn, Pharmacia, and Pfizer. And, it seems the lion’s share of these lawsuits involves three drugs, namely, Premarin (estrogen based), Provera (progesterin), and Prempro (a combination of the two hormones),²¹ all of which remain on the market (as of December 7, 2012). The account of HRT litigation offered here focuses on these three drugs.

The personal-injury claims involved in this litigation differ in several ways besides which of the drugs was alleged to have caused injury. These differences include the alleged type of injury (for example, breast cancer or heart attack), the time relative to the onset of menopause when the plaintiff’s therapy commenced, the duration of her HRT use, and so on.

A 2010 editorial in the *Journal of the American Medical Association*—Bach (2010)—provides a helpful, and only moderately technical, account of some of the key studies, and the summary of the scientific evidence provided in this paragraph relies on that editorial unless otherwise noted. HRTs were very widely used by American women for decades.²² In July 2002, a report of results from a large-scale clinical trial (Rossouw et al., 2002)—called the Women’s Health Initiative (WHI)²³—pertaining to combination estrogen-progesterin use by women aged 50 to 79 years with a uterus, with an average age of 63 years whose health was observed for an average of a little more than five years (Rossouw et al., 2002). This study reported that women

²⁰ A controversial aspect of the original settlement agreement was that lawyers with any clients enrolling in the settlement agreed to recommend participation to all of their eligible clients and “to take all necessary steps to disengage and withdraw” from continuing to represent clients who did not agree to participate (Merck & Co., Inc., and The Counsel Listed on the Signature Pages Hereto, 2007, p. 6; see also, Koppel, 2007; and Nagareda, 2008, p. 4). Rheingold (2008, supp. p. 74) describes resulting modifications of the settlement agreement and Rheingold (2008, supp. p. 75) expresses remaining ethical concerns: “It is somewhat disingenuous to defend [the proposition that] a requirement that the lawyer ‘recommend’ settlement is not the same as forcing it on the client . . . Independence of advice is lost.” Nagareda (2008, p. 4) argues, however, that such concerns are “at odds with the realities of client representation in the mass tort setting.”

²¹ In 2002, Pfizer merged with Pharmacia—which at that time owned Upjohn. Pfizer purchased Wyeth in 2009. Provera was an Upjohn and Pharmacia product. Premarin and Prempro were Wyeth products (Pfizer Inc., 2011a, p. 104).

²² See, for example, Majumdar, Almasi, and Stafford (2004, p. 1984) who report that by “the mid-1990s, almost half of all postmenopausal women in the United States were being prescribed long-term hormone therapy.”

²³ The study was stopped earlier than had been planned because of evidence of harm from the HRT.

receiving HRT experienced higher rates of breast cancer, myocardial infarction (heart attacks), stroke, and pulmonary embolism than women receiving a placebo. Very few of the subjects began participation in the trial near the time of menopause, however, and among those women who did commence therapy near the time of menopause there was some evidence that HRT may have slightly *reduced* their risks of cardiovascular disease. A later analysis of WHI data (Rossouw et al., 2007) analyzed effects of age and years since menopause when HRT was initiated among women who had had a hysterectomy. This study found some evidence that women who began HRT closer to menopause had lower rates of coronary heart disease than women who began HRT after more time had passed since menopause, but that the risk of stroke was elevated no matter when HRT was initiated (Rossouw et al., 2007). And in 2010, another study (Chlebowski et al., 2010) of WHI data, focusing on the same subpopulation studied in the 2002 report, found that after an average of 11 years of follow-up, the estrogen-progestin combination increased the incidence of breast cancer and (more tentatively) mortality from breast cancer.

The publication of the first WHI report (Rossouw et al., 2002) appears to have triggered a large number of product-liability personal-injury lawsuits, with about 3,600 filed during the following three years; about 3,000 of which were federal suits consolidated in an MDL (Selvin, 2005), namely, MDL 1507 *In re Prempro Products Liability Litigation*.²⁴ The first federal trial, which was part of the MDL, was held in 2006. The plaintiff (Linda Reeves) had apparently taken Premarin and Prempro for more than 15 years and subsequently developed breast cancer. She alleged a FTW, design defect, and other common-law causes of action (Tesoriero, 2006). The jury ruled in favor of defendant Wyeth (*APLR*, 2006).

As of February 2011, “Pfizer’s Wyeth and Upjohn units have lost eight of 15 Prempro trials decided by juries” (Feeley, 2011b). Trials have involved various injuries alleged to be caused by HRT use, some have involved punitive damages, and some jury verdicts have been overturned. Lawsuits brought against Pfizer or its subsidiaries as of the end of 2010 “have alleged breast cancer, ovarian cancer, stroke and heart disease,” as well as other injuries (Pfizer Inc., 2011a, p. 104). And the company subsequently reported (Pfizer Inc., 2011b, p. 27) that as of July 3, 2011, the company and its affiliates had settled or agreed to settle “approximately 41% of the hormone-replacement therapy actions” and that they had “recorded aggregate charges . . . of approximately \$250 million in the first six months of 2011 and \$300 million in prior years.” Finally, the company reported at the same time that its estimate of “the minimum expected costs to resolve all of the other outstanding hormone-replacement therapy actions” was “approximately \$280 million” (Pfizer Inc., 2011b, p. 27).

Zyprexa

Zyprexa is the brand name for olanzapine, one of several “second-generation atypical” (SGA) or antipsychotic or psychiatric drugs (Mossman and Steinberg, 2009). The product remained on the market in the United States as of the end of 2011 and is manufactured by Eli Lilly and Company. Zyprexa was approved by the FDA for U.S. marketing in 1996 for treatment of schizophrenia. Additional indications were subsequently approved, including acute bipolar mania in 2000.

²⁴ The federal MDL has involved as many as 9,600 cases with about 7,600 still pending as of January 2011 (Raymond, 2011a).

Some scientific evidence suggesting serious side effects of SGAs emerged in the late 1990s, and by 2002 there were reports “showing that, in addition to weight gain, SGAs were associated with abdominal obesity, elevated blood lipids, high blood pressure, and elevated fasting glucose” (Mossman and Steinberg, 2009, pp. 290–291, fn. omitted). In March 2004, manufacturers of several SGAs added or strengthened warnings about diabetes and high blood sugar (Waters and Fisk, 2007), and Zyprexa warnings were strengthened in October 2007 “citing the drug’s tendency to cause weight gain, high blood sugar, high cholesterol and other metabolic problems” (Berenson, 2007b).

Tens of thousands of lawsuits alleging personal injury from Zyprexa have involved a variety of alleged injuries and alleged bases for liability. Most of the lawsuits appear to involve claims of Zyprexa causing diabetes or high blood glucose (sugar) levels and allegations of failure to adequately study the drug’s side effects, FTW adequately prescribing physicians, and (less often) improper promotion of the drug (Eli Lilly and Company, 2005a, p. 13). In April 2004, most of the federal lawsuits involving Zyprexa were consolidated in an MDL and transferred to Judge Jack Weinstein in the U.S. Federal District Court for the Eastern District of New York (MDL 1596). As of the end of 2004, about 140 product-liability lawsuits alleging personal injury from Zyprexa, representing about 360 individuals, had been filed (Eli Lilly and Company, 2005a, p. 13).

Almost all of the Zyprexa lawsuits have been settled, abandoned, or dismissed. In January 2007, the manufacturer reportedly agreed to pay \$500 million to settle 18,000 lawsuits for cumulative totals at that time of at least \$1.2 billion to settle claims with about 28,500 claimants (Berenson, 2007a). The defendant has reported that as of the end of 2010, a total of about 32,720 Zyprexa claims had been settled, with the “two primary settlements” accounting for the bulk of this total. Specifically, these were a June 2005 settlement involving payments of about \$700 million to settle more than 8,000 claims²⁵ and a January 2007 settlement involving payments of about \$500 million to settle more than 18,000 claims.²⁶ As of the end of 2010, about 70 Zyprexa lawsuits were still pending in the United States involving about 150 plaintiffs (Eli Lilly and Company, 2011, p. 32).²⁷

Mass Tort Attempts Resulting in Substantially Smaller Payouts by Defendants

The case histories provided to this point could leave readers with the impression that when plaintiffs’ lawyers attempt to develop pharmaceutical mass torts, defendants typically make several hundreds of millions of dollars, if not billions, in indemnity payments. This is not the

²⁵ These were inventory settlements with 17 law firms listed in Eli Lilly and Company (2005b, pp. 22–23).

²⁶ These were also apparently inventory settlements.

²⁷ Large numbers of product-liability lawsuits have been filed alleging serious personal injuries from other SGAs. For example, tens of thousands of claims have been asserted alleging that Seroquel increases the risk of developing diabetes. The federal cases were consolidated in MDL 1769. In July 2011, Seroquel’s manufacturer (AstraZeneca) reported that it had reserved \$647 million to cover settlement of almost 28,500 such suits, roughly 250 additional claims that had not been settled, legal defense costs since October 1, 2010, as well as projected future legal costs (Feeley, 2011c). The company also reported that its defense costs incurred before July 2011 totaled almost \$750 million. Rheingold’s 2011 volume (p. 87), which was finalized before July of that year, refers to two settlements of federal cases totaling about \$350 million. Therein, Rheingold reported that the average settlement was about \$25,000, which he referred to as “a relatively small sum.”

case, however.²⁸ More specifically, sometimes these efforts result in billion-dollar settlements, and sometime these efforts largely fail from the plaintiffs' point of view in that they result in indemnity payments of roughly \$100 million or less.²⁹

In this section, I review in some detail two mass tort attempts by plaintiffs' lawyers to obtain large aggregate recoveries for their clients, namely, the Norplant litigation and attempts to obtain compensation for children with autism allegedly caused by vaccines.³⁰ The section concludes with much less extensive accounts of two other mass tort attempts, against Meridia and Serzone, that also seem to have largely failed to obtain large sums for claimants.

Norplant

Norplant is a contraceptive drug³¹ (levonorgestrel, a type of progestin), which was marketed by AHP, later renamed Wyeth. The drug is slowly delivered over the course of five years from six silicone rods that are implanted under the skin of a woman's upper arm. Norplant—"the first major new contraceptive since the birth control pill" (Cohen, 1995)—was approved by the FDA for sale in the United States in December 1990, and marketing commenced in February 1991. About one million U.S. women (Cohen, 1995; *The Economist*, 1995) received Norplant by 1995. During the first three years on the market, about 20 lawsuits alleging personal injury were filed against the manufacturer. As many as 50,000 women had become plaintiffs by late 1995 (Cohen, 1995). During that year, several mass media reports—including Cohen (1995), Cowley (1995), Kolata (1995), and *The Economist* (1995)—reviewed the history of Norplant, the rising tide of lawsuits, as well as support for the product by many physicians, scientists, regulators, and women's health groups. The injuries alleged to be caused by Norplant by 1995 included "a wide array of side effects: memory loss, muscle pain, depression, autoimmune disorders, infections, seizures, blindness, cancer and heart attacks—just to name a few" (Kolata, 1995).

Those four 1995 articles also reported substantial sales declines of the product after its peak-sales year of 1992. Kolata (1995) indicates that the manufacturer reported that sales had declined from about 800 to 60 systems per day because of "adverse publicity and negative word-of-mouth." The articles also discussed the possibility that the product would become unavailable because of the large volume of litigation. Sales of Norplant were suspended in 2000

²⁸ It is emphasized, however, that even if plaintiffs recover little money, the legal costs of defendants can be quite considerable, and legal costs are a component of the incentives affecting company decisions.

²⁹ Total indemnity payments involved in a particular mass tort vary over a continuum, of course. The dichotomy between "successful" and "failed" attempts is merely an expository device. There is at least one mass tort attempt during the 1990s and 2000s that doesn't fit into either of the two categories, namely OxyContin, a pain medication approved by the FDA in 1995 and marketed by privately held Purdue Pharma. By 2007, roughly 10,000 personal-injury claims were brought against Purdue—most apparently claiming insufficient warnings about additive potential and death from overdoses (Frankel, 2007). Two plaintiffs' firms that represented a total of about 5,000 claimants reportedly settled their cases at the end of 2006 for a total of \$75 million, and by July 2007 two other settlements totaled about \$40 million (Frankel, 2007). In February 2007, it was reported that the company had settled more than 1,000 other lawsuits, accounting for about 90 percent of the 1,374 remaining lawsuits, for a total of \$75 million (Mass Tort Litigation Blog, 2007).

³⁰ As detailed below, the latter litigation largely played out within administrative proceedings because of earlier federal legislation that established an administrative compensation program for injuries caused by childhood vaccines and also greatly reduced claimants' opportunities in tort actions.

³¹ Much of the commentary about Norplant, including many of the sources cited here, refer to Norplant as a "device." Technically, however, under FDA definitions, Norplant is a drug (and is regulated as a drug) because its (contraceptive) purpose is achieved through chemical action.

because of concern about reduced shelf lives in some batches, and in July 2002 the company announced in a letter to doctors that Norplant would no longer be sold in the United States (Johnson, 2002; Siegel Watkins, 2010, p. 104). While the company attributed this decision to supply problems with components, many attribute the lack of availability of Norplant to litigation costs and risks. And to the extent that the product was discontinued because of lack of profitability associated with depressed sales, the question becomes the role of litigation in generating “adverse publicity and negative word-of-mouth.” Thus, it is not entirely clear whether, absent product-liability exposure, Norplant would have remained available in the United States.³²

The Norplant lawsuits filed in federal courts were consolidated in 1994 (MDL 1038), which reportedly involved as many as 50,000 claimants. Norplant’s labeling listed 26 different potential side effects, and plaintiffs alleged that these warnings were inadequate, as well as alleging over 900 other injuries that they attributed to Norplant use (Harris, 2002). In September 1999, Wyeth announced that it had entered into settlement agreements with “plaintiffs’ counsel representing virtually all of the NORPLANT SYSTEM plaintiffs to settle then-pending NORPLANT SYSTEM lawsuits for \$1,500 per claimant,” and by the end of that year about 32,000 plaintiffs had accepted the offer, leaving about 5,000 plaintiffs who had not settled (AHP, 2001).³³ In August 2002, the MDL judge dismissed almost all of the roughly 3,000 remaining federal claims, ruling that the learned intermediary doctrine applied to the 26 potential side effects included in Norplant’s labeling³⁴ and that there was insufficient scientific evidence to support claims involving other injuries (Manson, 2002). The judge’s ruling (which was upheld on appeal) ended most of the Norplant litigation.

Childhood Vaccines and Autism

In recent years, there have been major controversies relating to the safety of childhood vaccines. Most prominently and importantly for present purposes is the possibility that thimerosal, a vaccine preservative, can cause autism or, more precisely, “autistic spectrum disorders” or “pervasive developmental disorders” (IOM, 2004, pp. 3–4). For expositional economy, I will simply use the term *autism*. As of 1999, thimerosal was widely used in vaccines administered in the United States, including some administered routinely to infants and children (IOM, 2004, p. 5). Since the early 2000s, childhood vaccines administered in the United States have not used thimerosal as a preservative, although some of these vaccines include trace amounts of thimerosal (U.S. FDA, 2010, Table 1). There has also been special concern about autism and vaccines for measles, mumps, and rubella (MMR) vaccine.

Thousands of legal claims have been brought for compensation for autism allegedly caused by vaccines administered to infants or children. Product-liability law pertaining to vaccines is very different than that applying to other pharmaceuticals. As detailed presently, there

³² Birenbaum (2001) provides more information about how the litigation and publicity about it likely caused many physicians and patients to choose not to use Norplant. She reviews a fairly persuasive case that Norplant is a safe, convenient, and effective contraceptive and that if it were not for product liability, Norplant would not have been withdrawn from the U.S. market.

³³ Not counting the claimants in a pending class action in Louisiana.

³⁴ In fact, the judge did not dismiss the ten claims to be adjudicated under New Jersey law and returned them to the courts in which they were filed, because under New Jersey law (*Perez v. Wyeth Laboratories*) products promoted through DTC advertising are excepted from application of the learned intermediary doctrine.

is an administrative program that provides compensation for some injuries associated with vaccinations, and access to compensation for vaccine-related injuries through the courts is substantially curtailed relative to that pertaining to other pharmaceuticals. We can only speculate about how a mass tort involving vaccines and autism would have played out under the legal rules that apply to other pharmaceuticals. Thus, the failure of this mass tort attempt from the plaintiffs' point of view may or may not be attributable to the special tort rules for vaccines as contrasted with difficulties in proving injury causation, which are emphasized presently.

The NCVIA of 1986 was adopted because of widespread concerns about shortages of childhood vaccines that were attributed, at least in part, to product-liability exposure (Congress of the United States, Office of Technology Assessment 1979; IOM, 1985). The act authorized a no-fault compensation program—the Vaccine Injury Compensation Program (VICP)—for some injuries emerging after vaccinations and protected vaccine manufacturers from liability in hope of assuring national access to new vaccines (Mariner, 1992; Johnson, Drew, and Miletich, 1998; Mello and Brennan, 2005). In particular, compensation is typically readily available through the program if the claimant can show, as specified in the Vaccine Injury Table (U.S. Department of Health and Human Services, Health Resources and Services Administration, undated), that (1) a vaccine covered by the program was administered to the injured person, (2) the injury or “adverse event” that occurred is listed as compensable for that vaccine, and (3) the injury began to manifest within a specified time interval after the vaccine was administered. Listed adverse events and time intervals are based on consensus scientific views and are periodically updated as new studies become available (Sugarman, 2007, p. 1276).

Autism is not listed as a qualifying adverse event for any vaccine (Sugarman, 2007; U.S. Department of Health and Human Services, Health Resources and Services Administration, undated). As a result, claimants seeking compensation for autism through the VICP—as for all claimants seeking compensation for injuries not satisfying the criteria for no-fault compensation listed in the vaccine injury table—must prove that the injury resulted from the vaccination. With very few exceptions, those seeking compensation for autism have been unsuccessful in this regard (Stobbe and Marchione, 2008).

In order to have any access to the courts, a claimant must first file a petition with the U.S. Court of Federal Claims seeking compensation through the VICP. If a claimant finds the award unacceptable, or there is no award (as has been the case with virtually all autism claims), the claimant may pursue product-liability or other legal claims in state or federal court (Stewart, 2009). When claimants do so, however, defendants enjoy (under NCVIA) several legal protections that were succinctly stated by the U.S. Supreme Court in its decision in February 2011 in *Bruesewitz v. Wyeth*, in which the issue was implications of NCVIA for the availability of design-defect claims. Specifically, the opinion reads:

Manufacturers are generally immunized from liability for failure to warn if they have complied with all regulatory requirements (including but not limited to warning requirements) and have given the warning either to the claimant or the claimant's physician. They are immunized from liability for punitive damages absent failure to comply with regulatory requirements, “fraud,” “intentional and wrongful withholding of information,” or other “criminal or illegal activity” (Supreme Court of the United States, Opinion of the Court, 2011a, pp. 4–5).

And the court ruled “we hold that the National Childhood Vaccine Injury Act preempts all design-defect claims against vaccine manufacturers brought by plaintiffs who seek compensation for injury or death caused by vaccine side effects” (Supreme Court of the United States, Opinion of the Court, 2011a, p. 19).

Safety concerns about thimerosal were greatly heightened in 1999 when FDA researchers found that the amount of one kind of mercury (ethylmercury) included in recommended vaccinations could exceed federal guidelines for exposure to a different form of mercury (methylmercury), and the Academy of Pediatrics and the U.S. Public Health Service “issued a joint statement recommending removal of thimerosal from vaccines as soon as possible” (IOM, 2004, p. 5). Concerns about the MMR vaccine, which did not use thimerosal as a preservative, and autism stem largely from a discredited and retracted (see, for example, Wang, 2010) study. The study (Wakefield et al., 1998) was published in the *Lancet* (a very prestigious British medical journal). A committee of IOM examined the scientific evidence concerning MMR and autism and thimerosal and autism and concluded in 2004 that

the body of epidemiological evidence favors rejection of a causal relationship between the MMR vaccine and autism. The committee also concludes that the body of epidemiological evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism. The committee further finds that potential biological mechanisms for vaccine-induced autism that have been generated to date are theoretical only (IOM, 2004, p. 1).

The basic contours of vaccine-autism claiming and litigation are as follows. As of 2009, more than 5,300 autism-related claims were pending with the vaccine injury compensation program (Stewart, 2009, p. 2498), and virtually all of these claims had been filed since 2002 (Sugarman, 2007, figure 1). In June 2002, GeneralCologne Re (2002, p. 1) asserted that “Childhood vaccines are the latest lightning rod for widespread pharmaceutical litigation.”

It appears that several pharmaceutical companies received numerous claims for compensation. These companies include Merck and Eli Lilly, which reported to stockholders some quantitative information during the mid-2000s. For example, at the end of 2005, Merck reported approximately 275 active thimerosal suits involving about 775 plaintiffs, and for the end of 2010, 110 lawsuits, “although the vast majority of those lawsuits are not currently active” (Merck & Co., 2006, p. 30; 2011 p. 132). As of the end of 2005, Eli Lilly had been named in about 340 lawsuits in the United States involving about 1,020 claimants “on behalf of children with autism or other neurological disorders,” and the corresponding figures for the end of 2010 were 120 lawsuits and 140 claimants (Eli Lilly and Company, 2006, p. 16; 2011, p. 14).

Litigation involving personal injuries from vaccines raise two kinds of issues pertaining to potential effects on public health. First, despite the reductions in liability exposure under NCVIA, many commentators remain concerned about liability being a threat to vaccine supply and availability. For example, Noah (2003, pp. 759–764) argues for further lessening of liability exposure for manufacturers, while also arguing that strict regulation of manufacturing processes and facilities and efforts to control health care costs are also major factors undermining the profitability of the vaccine business. Offit (2005) likewise points to various factors

undermining vaccine supply, including liability. He argues that the NCVIA does not go far enough in protecting manufacturers from liability.³⁵

The second public health concern pertains to effects of litigation, which publicizes safety concerns—whether grounded in reliable scientific evidence or not—on the willingness of parents to have their children vaccinated. More specifically, concerns about vaccine safety—in many cases, about autism—seem to have contributed to reduced immunization rates for some diseases in some places in the United States and outbreaks of diseases that are largely preventable through vaccination (Steinhauer, 2008).

Other Mass Tort Attempts That Have Largely Failed for Plaintiffs

In addition to Norplant and litigation alleging autism caused by vaccines, other recent mass tort attempts seem to have largely failed from the plaintiffs' point of view. Three of these are briefly discussed here.

Meridia is a weight loss drug that had been marketed in the United States from FDA approval in 1997 (at the time by Knoll Pharmaceuticals) until October 2010, when it was removed from the market by Abbott Laboratories, which had bought Knoll in the interim (U.S. Court of Appeals for the Sixth Circuit, 2006; Abbott, 2010). The federal cases, many of which alleged that the drug caused heart and circulatory problems, were consolidated and transferred in August 2002 to MDL 1481 (*APLR*, 2002a; Frankel, 2006). In 2004, the MDL judge dismissed all of the roughly 100 pending cases, ruling that the product warnings were adequate (invoking the learned intermediary doctrine), and the Sixth Circuit upheld the ruling in 2006 (Rheingold, 2006, sec. 3:20). Rheingold (2006, sec. 3:20) also reports that the judge's grant of summary judgment was preceded by a successful *Daubert* challenge to plaintiffs' experts' testimony.

Finally, thousands of product-liability claims have been brought claiming personal injury from *Serzone*, an antidepressant drug. The alleged injuries involved a small number of cases with serious liver damage. In 2008, 3,681 claims in the federal MDL (1477) were settled for \$31.27 million, with almost 3,000 of the cases (which involved less serious injuries) settled for \$100 per case (Rheingold, 2011, p. 87).

Summing Up

This review of largely resolved mass tort attempts during the 1990s and 2000s suggests several conclusions about economic effects of personal-injury, product-liability claims against pharmaceutical manufacturers.

Mass Drug-Related Injuries

Mass injuries actually or allegedly caused by prescription drug use have remained a major social concern. It is unclear, however, what proportion of such injuries are attributable to man-

³⁵ It appears, however, that more recently manufacturers have become more enthusiastic about the profit potential of vaccines (Zachary, 2007). The role, if any, of product-liability developments in increasing willingness to develop and supply vaccines is unclear.

manufacturer behavior that, according to legal doctrine, makes them legally liable. For example, manufacturers are not legally liable for types of injuries about which they provided legally adequate and timely warnings.³⁶

It is also unclear how many drug-related injuries have been associated with drugs involved in mass torts. To develop a sense of the extent of serious drug-related injuries, consider the following. Let's assume that—with the exception of the Fen-phen litigation, in which many settled claims were not supported by reliable evidence of injury—settled personal-injury claims involved true injuries. Then, for example, at least 3,000 Baycol claimants suffered serious injury (settled claims for rhabdomyolysis), as did thousands of claimants in the Rezulin (liver damage) and HRT (including breast cancer and heart attacks) mass torts. Moreover, tens of thousands of claims were settled in Vioxx (heart attacks and ischemic strokes) and Zyprexa (elevated blood glucose levels and diabetes).

Mass Torts

Attempts to develop new mass pharmaceutical torts continued throughout the 1990s and 2000s. As highlighted in this chapter, some of these attempts have resulted in very large aggregate payouts to claimants, and others have resulted in much smaller payouts. There is no reason to expect that—absent federal legislation preempting PPL claims—such mass tort attempts will cease any time soon.

Financial Incentives to Avoid Liability

As illustrated by several of the mass tort histories, the potential cost of a mass tort to its manufacturer is in the billions of dollars. It seems obvious intuitively that the possibility of a future mass tort is a sufficient financial threat to attract the attention of company decisionmakers and lead them to consider responses to the possibility. More specifically, company decisionmakers should be expected to consider ways to reduce the likelihood of a mass tort attempt involving one of their products, the company's likely cost if such an attempt is made, or both. This conclusion can be supported analytically as follows.

As argued in Chapter Two, company decisionmakers are likely to consider changing their behavior if they perceive an opportunity to reduce future expected liability costs by more than what it would cost the company to change its behavior. Different kinds of actions (or changes in behavior) might be considered by company decisionmakers seeking to reduce future personal-injury, product-liability costs. For example, adding warnings to a drug's label could, in principle, make the difference between a mass tort costing its manufacturer billions of dollars and a much less costly mass tort attempt or no mass tort attempt at all. For another example, reporting information from clinical trials or adverse event reports more completely and accurately to the FDA could also greatly reduce a company's expected liability cost because evidence of failure to comply with regulations can greatly increase damage awards. For both of these examples, the primary cost of lowering expected liability costs might be the same—namely, lost sales of the drug—but the reduction in expected liability cost and the costs of

³⁶ Undoubtedly, factors other than FTW contribute to the persistence of mass drug-related injuries. These factors may include (1) many of the drugs involved in mass tort attempts are used to treat chronic conditions or risk factors that affect or are diagnosed for massive numbers of people (obesity, high cholesterol, arthritis), and sometimes for long periods of time, (2) drugs must be somewhat toxic to be effective, and (3) some drugs will cause injuries even when all socially worthwhile efforts to reduce risk are taken. The relative importance of these explanations of mass drug-related injuries is far from clear.

gaining this benefit might differ greatly across the two approaches (which are not mutually exclusive).³⁷

We should expect, then, that company decisionmakers will respond to the threat of a mass tort in whatever ways that they think will reduce their future liability exposure with acceptable implications for profitability. Regarding attracting the attention of company decisionmakers, it may suffice merely to observe that some recent mass torts (Fen-phen and Vioxx) have cost manufacturers billions of dollars, and it is hard to imagine that anyone who makes liability-related decisions for a pharmaceutical company is unaware of this. In sum, we should expect company decisionmakers to go to considerable lengths to avoid behavior that they view as substantially increasing the likelihood that any particular drug will be the target of an attempt to develop a mass tort.

Roles of Punitive Damages

Punitive damages have been awarded in several of the mass torts reviewed. And even if many or most punitive awards are reduced or eliminated by the trial judge or on appeal, company decisionmakers are likely to view potential punitive damages as highly salient. While recent Supreme Court decisions aimed at lowering the size of punitive damages in any one case may have lessened the expected costs of punitive damages somewhat, potential punitive damages will most likely continue to loom large in the minds of decisionmakers. First, in the mass tort context, punitive damages can be awarded in multiple trials for the same behavior. Second, as emphasized in Garber (1993, pp. 196–197) and Garber (1998, pp. 256–257), the vagueness of the standards for availability of punitive damages in many states strongly suggests that decisionmakers face major uncertainties about the specific behavior or actions that will or will not expose their companies to punitive damages. Regarding implications for company decisions and economic outcomes, punitive damages may be viewed in large measure as increasing the stakes involved when mass torts are attempted, thereby strengthening incentives to respond to liability exposure. In short, we should expect that potential punitive damages tend to increase behavioral responses of manufacturers, whether these effects are socially desirable or the opposite (Garber, 1998, pp. 255, 285).

Controversies About Injury Causation

Controversies about injury causation have been a central feature of several mass torts. It is not clear whether more-extensive judicial gatekeeping for expert testimony since the Supreme Court's decision in *Daubert* has had any substantial effect on the likelihoods that defendants will be held liable in the absence of reliable evidence on injury causation,³⁸ or whether plaintiffs will be disadvantaged by unreliable evidence offered by defendants. Most importantly, there is

³⁷ The line of reasoning used in the text uses a private rather than societal cost-benefit (for company finances) perspective to consider whether and how companies are likely to respond to their perceived liability exposure. Other perspectives—albeit ones not aimed at predicting company responses—might help some readers put potential liability costs and savings in liability costs in perspective. For example, *Drugs.com* (undated) reports 2010 U.S. sales figures for top-selling drugs, and sales of the top ten ranged from \$2.6 to \$5.3 billion. Estimated 2011 figures for Pharmaceutical Research and Manufacturers of America (PhRMA) member companies (PhRMA, 2011, pp. 36–37, 42, 48) indicate that domestic sales per member were just about \$5 billion and domestic R&D was a bit shy of \$1 billion per company. (Including R&D conducted abroad adds about another 32 percent to this \$1 billion figure.)

³⁸ Perhaps the best-known example of a pharmaceutical mass tort attempt in the absence of substantial causation evidence is Bendectin; see Green (1996) and Sanders (1996).

no indication that unreliable evidence has been largely eliminated or that reliable evidence is rarely excluded.

Transaction Costs of Unsuccessful Mass Tort Attempts

Some mass tort attempts fail from the plaintiffs' point of view, but nonetheless generate substantial transaction costs for defendants and plaintiffs' lawyers. It appears that attempts fail for two main, interconnected reasons, namely, lack of sufficient evidence of either injury causation or FTW based on knowledge existing at the times that warnings were given. It is not clear whether policy changes could reduce the likelihood of similar future episodes. For example, it may be that a leading cause of failed mass tort attempts is that plaintiffs' attorneys have strong incentives to be among the first to file claims in a new mass tort. Such incentives include the increased likelihood that a plaintiff's firm will help establish an AAJ litigation group,³⁹ which in turn may help it attain leadership roles in the litigation (for example, by being included on the plaintiffs' steering committee for an MDL). Such "races to the courthouse" may often leave little time for attorneys to consider and truly understand what is known about a drug's risks and whether warnings were legally adequate.

The next chapter also pertains to personal-injury, product-liability litigation against pharmaceutical companies. Specifically, it reviews the policy debate concerning the economic pros and cons of preempting FTW PPL claims and assesses the state of empirical evidence about economic effects. Thus, the issue addressed in the next chapter pertains to the costs and benefits of almost all PPL litigation.

³⁹ AAJ litigation groups are voluntary alliances or networks of AAJ members who represent plaintiffs in similar lawsuits (or have an interest in doing so). AAJ members' main functions are to share information and foster cooperation among group members with the aim of helping plaintiffs' attorneys strengthen their cases and prevail over defendants in mass litigation settings (AAJ, 2012). In January 2012, there were almost 70 active groups, including many focused on particular pharmaceuticals, including Avandia, Chantix, Fosamax, Heparin, Meridia, and Neurontin, as well as groups focused on multiple similar drugs, including hormone therapies, Vioxx/Bextra (and other Cox-2 inhibitors), and vaccines (AAJ, 2012).

Preemption of Pharmaceutical Failure-to-Warn Claims

In November 2008, the U.S. Supreme Court heard oral arguments in *Wyeth v. Levine*,¹ in which pharmaceutical manufacturer Wyeth petitioned the court to rule that FTW claims against drug manufacturers are preempted (i.e., precluded or barred) by federal law. Simply put, the issue is whether state-law FTW claims are allowed under federal law. If such claims were barred, then plaintiffs (with the exception of cases involving vaccines) would have no recourse because there is no cause of action available under federal law in such cases.

Since the lion's share of PPL cases involves, in fact, FTW cases, a ruling in favor of the petitioner might have barred most product claims against drug manufacturers.² In March 2009, the Supreme Court ruled against Wyeth, finding that Levine's claims were not preempted.³

In this chapter, I discuss major *economic* issues pertaining to the social costs and benefits of preempting FTW claims. By way of background, I begin with a discussion of federal preemption law.

Federal Preemption Law

The fundamental legal question that arises in the context of federal preemption of state law is whether Congress intended to preempt. Discussions of federal preemption typically distinguish between *express* preemption—instances in which the language in a federal statute explicitly says that state law is preempted⁴—and *implied* preemption—instances in which the statute does not contain explicit preemption language, but courts nonetheless find that Congress intended to preempt. Different legal scholars categorize and describe types of implied preemp-

¹ All references to “*Wyeth v. Levine*” in this study refer to the U.S. Supreme Court case (rather than cases of the same name in lower courts).

² As discussed presently, the fundamental issue in federal preemption law is whether Congress intended to preempt state law. Thus, a U.S. Supreme Court ruling in favor of Wyeth would not necessarily have barred FTW claims forever or even for an extended length of time because Congress could have allowed such claims through new legislation.

³ The drug in question in *Wyeth v. Levine* was a brand-name drug (i.e., not a generic version of a brand name drug whose patent had expired). As discussed below, in light of the U.S. Supreme Court decision in *Pliva, Inc. et al. v. Mensing* on June 23, 2011, this distinction has proved to be crucial.

⁴ In fact, and despite some commentary suggesting otherwise, the U.S. Supreme Court preemption ruling in *Riegel vs. Medtronic* that involved a medical device did not provide much guidance, since that ruling was based on explicit preemption language in the *Medical Device Amendments of 1976*. There is no express preemption language in the law pertaining to pharmaceuticals.

tion in different ways.⁵ For present purposes, the key point is that economic considerations are relevant to the legal debate to the extent that they fit into the legal framework.

Despite the fact that it is up to Congress to preempt, the controversy addressed in *Wyeth v. Levine* has come to be known as the “FDA preemption” issue. This is because in January 2006, the FDA asserted within its new, final *Physician Labeling Rule* that the rule preempts conflicting state laws (such as FTW product-liability claims), writing, for example, “FDA believes that under existing preemption principles, FDA approval of labeling under the act . . . preempts conflicting or contrary state law” (U.S. Department of Health and Human Services, Food and Drug Administration, 2006, p. 3934).⁶ It seems widely agreed that (1) the key issue was whether Congress intended to preempt state-law claims involving FTW,⁷ and (2) Congress had the authority to change the relevant legislation if it was not satisfied with the Supreme Court decision.⁸ The FDA assertion of preemption led to a large volume of writing—including law review, medical journal, other scholarly articles, and legal briefs—on the pros and cons of preempting lawsuits claiming FTW on the part of drug manufacturers. Much of this literature focuses on legal⁹ or political issues.

Purported Economic Effects of Failure-to-Warn Claims

The focus here is on the likely economic effects of preempting FTW claims, and some recent writing on preemption provides an opportunity to assess the state of the policy debate and associated empirical information on this subject. More specifically, several *amici* briefs filed with the U.S. Supreme Court in *Wyeth v. Levine*—some arguing for preemption and others arguing against—emphasize putative economic effects of FTW product-liability claims against phar-

⁵ Schuck (2008) and Epstein (2009) offer different, but not necessarily incompatible, accounts. More specifically, Schuck (2008, p. 80) writes: “Conflict preemption occurs when the demands of the regulatory scheme are inconsistent with the demands of tort law—where it is impossible for a private party to comply with both state and federal requirements, or where state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.” And Epstein (2009, p. 464; emphasis in the original) writes, “the common view holds that there are three possible grounds for *implied* preemption. The strictest standard allows for preemption only in cases of *actual conflict*, such that there must be a clear inconsistency between what the federal government and the state government each allow or require. Second, it is often stated that the preemption in question only arises in those cases where the imposition of the state liability will *frustrate* the ends of the federal statute. Finally, a third form of preemption argues that preemption does not require this form of explicit conflict, but is satisfied if it appears that the federal statute has *occupied the field*, blocking state efforts to impose sanctions within that field even if there is no explicit conflict.” Mendelson (2008) discusses preemption doctrine and the view that there is a “presumption against preemption” in the context of federal agencies asserting preemption.

⁶ A major purpose of the new rule was to “make it easier for health care practitioners to access, read, and use information in prescription drug labeling” (U.S. Department of Health and Human Services, Food and Drug Administration, 2006, p. 3922). In large measure, the rule was hoped to mitigate the problem of “overwarning” (discussed later in this chapter) embodied in official drug labeling (package inserts) before the new rule was instituted.

⁷ Although the preemption issue was considered by the Congress, the FDAAA of 2007 does not contain any (express) preemption provision (Kessler and Vladeck, 2008, fn. 27, p. 468).

⁸ See Sharkey (2007b)—who considers preambles asserting preemption by the Consumer Product Safety Commission and the National Highway Traffic Safety Administration as well as the FDA—for a broader perspective.

⁹ One controversial issue is whether preemption would or should apply when the defendant is alleged to have committed fraud on the FDA—and, if not, what institution should make the judgment about whether fraud was committed. In *Buckman Co. v. Plaintiffs’ Legal Committee*, the U.S. Supreme Court found implied preemption of state law claims alleging fraud on the FDA. See Sharkey (2008) for a discussion and analysis in the context of agency preemption.

maceutical manufacturers. From a legal perspective, economic effects are important in considering whether and to what extent FTW claims conflict with the objectives of FDA regulation of prescription pharmaceuticals. In view of the apparently high stakes in the Supreme Court's decision in *Wyeth v. Levine*, *amici* who address economic effects were likely motivated to make their cases as strongly as they were able.¹⁰

Table 5.1 summarizes economic arguments raised for and against preemption in two recent articles—one arguing for and the other arguing against preemption—and eight *amici* briefs filed in *Wyeth v. Levine*—four of which argue for preemption and four of which argue against preemption.¹¹ The ten documents summarized in Table 5.1 were selected because they are all fairly recent and emphasize economic effects,¹² make relatively clear and direct claims about such effects, and, in many instances, cite other sources for supporting empirical evidence. The table also reports *empirical* studies cited in the various briefs. This information is included because it is helpful to policymakers and analysts seeking to understand the nature of the evidence on economic effects. For example, some of the cited sources contain (more or less persuasive) empirical information, others involve inferences based on cogent (more or less empirically grounded) economic logic, and others involve only unsubstantiated assertions.¹³

Table 5.1
Claimed Economic Effects of Pharmaceutical Failure-to-Warn Liability in FDA Preemption Debate

Document	Principal Claimed Economic Effects of Liability (page)	Elaborations and Examples (page); [empirical studies cited]
Supporting Preemption		
Article		
Troy (2007)	(i) "stifles innovation" (ii) "reduced the availability of drugs" (iii) "higher drug prices" (iv) harming public health though inappropriate warnings (p. 86)	(i) Innovation: R&D expenditures higher when liability costs and/or liability risks lower (p. 87) [Finkelstein (2003), vaccine R&D; Garber (1993), generally]; slowing development of contraceptives and AIDS vaccines. (ii) Availability: withdrawal of Bendectin ("the signal example") from market (pp. 88–89) [Lasagna (1991)]; exit from vaccine market by several manufacturers and withdrawal of vaccine for Japanese encephalitis (p. 89) [Lasagna (1991)]. (iii) Prices: oral polio vaccine, DPT vaccine [Lasagna (1991), Garber (1993), Manning (1994, 1997)]; "Obviously, higher prices for drugs lead to decreased access to those drugs, curtailing the public health benefit of those drugs" (p. 90). (iv) Warnings: "liability system interferes . . . with providing physicians with the information necessary to make rational prescribing decisions" (p. 90) ". . . by creating an incentive for drug manufacturers to include warnings relating to all possible risks, even those that are trivial, extremely rare, or unproven" (p. 91).

¹⁰ As one might expect because the briefs were submitted within an advocacy process, those arguing for or against preemption did not acknowledge the possibility that economic effects they did not address support the opposite position.

¹¹ Many other sources claim or discuss such effects, but the documents summarized in the table raise the principal arguments.

¹² Many other articles about FDA preemption and *amici* briefs in *Wyeth v. Levine* focus on legal issues that are not considered in this study.

¹³ For example, there are instances in *amici* briefs filed in *Wyeth v. Levine* where a citation purported to support a claim about an economic effect is to a law review article that merely asserts that alleged economic effect without empirical substantiation or citation to a source that provides such substantiation.

Table 5.1—Continued

Document	Principal Claimed Economic Effects of Liability (page)	Elaborations and Examples (page); [empirical studies cited]
<i>Amici</i> briefs in <i>Wyeth v. Levine</i> (supporting petitioner Wyeth)		
PhRMA (2007)	(i) "These suits threaten the public health by deterring innovation and by interfering with FDA's regulation of drug safety and efficacy" (p. 8). (ii) "Unnecessary proposals for labeling changes will interfere with FDA's operations" (p. 13).	(i) Vaccines, contraceptives, drugs for rare diseases (p. 12); Bendectin as an example of a socially advantageous product withdrawn from the market despite lack of scientific evidence supporting plaintiffs' claims of birth defects (pp. 12–13). (ii) "Unnecessary warnings deter doctors and patients from using beneficial drugs"—referring (p. 15) to two focus groups and national survey of physicians conducted by the FDA [U.S. Department of Health and Human Services, Food and Drug Administration, 2000].
PLAC and USCC (2008)	"As a result [of many courts not finding preemption of FTW claims], the public health has been endangered" (p. 3).	"additional [to warnings viewed as appropriate by the FDA] requirements for the disclosure of risk information [that plaintiffs argue should have been provided] . . . can erode and disrupt the careful and truthful representation of benefits and risks that prescribers need to make appropriate judgments about drug use" (p. 5).
Calfee et al. (2008) ("economists and economics professors who teach and write on the economic impacts of regulation, including pharmaceutical regulation, and on health care policy") (p. 1).	(i) "Incentives facing FDA regulators result in excess caution in drug approval" (p. 6). (ii) "The same perverse incentives result in excess caution by FDA in drug labeling" (p. 10). (iii) "State tort product liability lawsuits exacerbate the problems of FDA's excess caution" (p. 13). {subsection headings; capitalization modified}	(i) The FDA is excessively cautious because the agency is much more likely to be criticized for approving a drug that is subsequently alleged to cause widespread injury (which would be highly visible) than for failing to approve a socially beneficial drug or delay its approval (which would be less widely appreciated) (pp. 6–8); "[y]et the adverse public health impact of a failure to approve a beneficial drug may be even more severe than the approval of an insufficiently safe drug" (p. 8). Examples of criticism of the FDA for approving drugs: SSRIs, Vioxx, IOM (2007) (p. 8); Philipson et al. (2008). (ii) "[T]wo adverse consequences would follow [from labels warning about, e.g., all possible side effects] . . . overwarning . . . which could deter or discourage drug use that would be beneficial . . . and 'clutter': the presence of so much information that physicians would find it hard to distinguish important information from relatively unimportant information and might not bother to peruse all the information" (p. 11). (iii) "In state tort lawsuits, juries necessarily focus on the highly specific personal tragedy rather than on societal tradeoffs . . . the jury balance will be skewed in favor of more warnings" (p. 13). "1. Limiting drug availability" through liability-induced (a) price increases that reduce product use (example is DPT vaccine) and (b) product withdrawals (examples are various companies ceasing to produce vaccines and Bendectin). "2. Disincentives for research & development" example: contraceptives. "3. Loss of FDA control over drug labeling" ". . . thus depriving the medical community in all states of the benefits of FDA expert determinations on proper and balanced drug warnings" (p. 17). "4. Defensive labeling" ". . . [t]he effect would be to discourage beneficial use of drugs whose labels contain these litigation-induced contraindications and warnings" (p. 18); example: erectile dysfunction drugs (p. 18). "5. Problems exacerbated further in state tort cases alleging missing contraindications" . . . "Physicians are likely to view contraindications as outright bans. . . . Then patients who would have benefited from the contraindicated use will be denied those benefits even if the expected benefit greatly exceeds the likelihood of harm" (pp. 19–20).

Table 5.1—Continued

Document	Principal Claimed Economic Effects of Liability (page)	Elaborations and Examples (page); [empirical studies cited]
DRI (2008)	<p>“[T]he absence of pre-emption encourages numerous negative effects, including (1) increasing defensive labeling to the detriment of optimal patient care, (2) discouraging manufacturers from bringing needed medications to market for fear of liability, (3) encouraging manufacturers to withdraw needed medications from the United States market even though they are available abroad, and (4) increasing prices for those drugs that remain on the market” (p. 4).</p>	<p>(1) “FDA has recognized that state law liability for failure to warn creates incentives for drug companies to engage in ‘defensive labeling’ As a result, beneficial drugs may be underutilized out of unwarranted fears or may be used when they should not be because physicians cannot distinguish the defensive labeling from the unsubstantiated risks” (p. 28).</p> <p>(2) “[T]here is a perverse incentive for the manufacturer to cease innovation, particularly for those drugs that are least profitable or pose the highest degree of risk (p. 30).</p> <p>(3) “Similarly, the threat of state-law liability for complying with FDA’s determinations creates incentives for manufacturers to restrict drug uses or to withdraw approved drugs from the market” (pp. 31–32); examples provided: Bendectin (Lasagna, 1991), Norplant.</p> <p>(4) “[H]igher prices may be the natural outcome” (p. 33).</p>
Opposing Preemption		
Article		
Kessler and Vladeck (2008)	<p>“Top-down surveillance [by the FDA] is no substitute for failure-to-warn litigation, which provides the FDA, doctors, and patients with information about new risks that is otherwise unavailable to the agency” (p. 484).</p>	<p>Several purported examples of important safety information about Rx drugs unearthed through liability litigation—Celebrex, Vioxx, olanzapine (Zyprexa), Halcion, Zomax, Paxil, other SSRIs (pp. 492–494) [Kesselheim and Avorn (2007)].</p>
Amici briefs in Wyeth v. Levine (supporting respondent Diane Levine)		
Carpenter et al. (2008) (“professors who teach and write on the politics and economics of pharmaceutical regulation and physician-researchers who study prescription medication use and policy” (p. 1).	<p>“Crucial information about a drug’s safety may become available only as a direct result of failure-to-warn litigation” (p. 7).</p> <p>“[T]he tort system encourages manufacturers to act reasonably in warning physicians and patients about newly emerging risks and helps ensure that important risk information is provided to physicians, patients, and the FDA” (pp. 7–8).</p>	<p>“Litigation brought by individual patients can help uncover previously unavailable data on adverse effects, questionable practices by manufacturers, and flaws in regulatory systems” (p. 17); Kesselheim and Avorn (2007).</p> <p>“Plaintiffs’ failure-to-warn suits give lawyers an economic incentive to gather information that national regulatory bodies lack” (p. 17).</p>

Table 5.1—Continued

Document	Principal Claimed Economic Effects of Liability (page)	Elaborations and Examples (page); [empirical studies cited]
California Medical Association (undated)	<p>(i) Preemption “would significantly weaken manufacturers’ incentives to conduct new safety studies, to monitor their drugs in the marketplace, to improve them post-approval, and to supply FDA and doctors with new or revised safety information” (p. 3).</p> <p>(ii) Preemption “may subject [doctors] to new and unwarranted liability for the consequences of drug defects . . . and could well drive some physicians from the profession” (p. 3).</p> <p>(iii) “Since they have not shown that ‘overwarning’ even exists in this context, Wyeth’s <i>amici</i> have not demonstrated that alleged ‘overwarning’ has led to underuse of prescription drugs” (p. 4).</p>	<p>(i) “Drug manufacturers who have, or could, obtain information about increased risk that would otherwise have to be disclosed would be protected from the consequences of their failure to disclose. This is true even if one believes that FDA has superior expertise in determining drug warnings’ contents” (p. 12).</p> <p>“[P]reemption of failure-to-warn claims [against drug manufacturers] threatens to shift liability for adverse drug side effects to physicians. . . . Such a shift may even force some doctors to abandon their practices” (p. 16).</p> <p>(ii) “Were this Court to preempt failure-to-warn claims, it would reduce significantly the incentive for drug companies to supply doctors and FDA with critical safety information and cut off information generated in pharmaceutical litigation. . . . it will become increasingly difficult for physicians to obtain the full and accurate information they must have to treat their patients safely. Consequently, patient safety will suffer” (pp. 19–20).</p> <p>(iii) “There is likewise little actual danger that including allegedly trivial or unsubstantiated information in a drug label would so thoroughly confuse doctors about real dangers that they would be too confused to utilize a drug properly” (p. 22). “In short, Wyeth’s <i>amici</i> cannot show any connection between alleged overwarning and alleged prescription drug underuse because there is not one” (p. 35).</p>
Members of Congress (2008)	<p>“Manufacturers should be given the incentive to supply the FDA with the most current evidence so that labels reflect the best scientific information. Congress understands that state tort law is an indispensable partner to federal safety regulation” (p. 4).</p> <p>“In addition, the FDA lacks the administrative resources to safeguard drug safety without the assistance of state-court lawsuits” (p. 5).</p>	<p>“When a drug is approved, the available information is not sufficient to guarantee its safety over time. . . . Many features of drug testing, production and marketing can result in new and unexpected risks once a drug enters widespread use, and these dangers are often solely within a manufacturer’s knowledge” (p. 25).</p> <p>“A long series of congressional hearings and reports has documented that the FDA’s resources are not commensurate with the agency’s enormous task” (p. 26).</p> <p>“The FDAAA of 2007 is intended to address these deficiencies, but it is not a panacea” (p. 27).</p> <p>“By necessity, manufacturers play a central role in the development and dissemination of information about their products. Accordingly, cases brought by injured consumers under state law can help ensure that manufacturers have the incentive to provide the most up-to-date warning information” (p. 28).</p> <p>“State tort cases also provide an invaluable source of data for regulators. Time and time again, problems with long-term use of drugs were identified first in failure-to-warn litigation, involving such drugs as Vioxx, Bextra, Celebrex, Avandia, Rezulin, Baycol, Halcion, and Zomax” (p. 28).</p>
New England Journal of Medicine Editors and Authors (2008)	<p>“[T]he FDA is in no position to ensure the safety of prescription drugs” (p. 3).</p>	<p>“Without the tort system, the FDA would be stripped of an essential source of information that the agency has consistently relied on when making its regulatory decisions, and the American public would be deprived of a vital deterrent against pharmaceutical company misconduct” (p. 5). “[D]rugs requiring complete withdrawal from the market for safety reasons are not rare” (p. 11). Examples of dozens of such drugs are tabulated in Appendix A. Examples discussed at length are Redux/Pondimin, Vioxx, and Trasylol (pp. 11–30).</p>

Economic Arguments Supporting Preemption

As detailed in Table 5.1, the article and four *amici* briefs arguing for preemption claim that several economic effects of pharmaceutical product-liability FTW claims are socially undesirable. Let's proceed to summarize these claims and assess the strength of available empirical evidence.¹⁴

Reduced Product Availability

Four of the five documents—the exception is Product Liability Advisory Council, Inc. and U.S. Chamber of Commerce (PLAC and USCC) (2008)—claim that product-liability exposure has limited the availability in the United States of drugs that have already been developed and whose lack of availability undermines public health and, thus, the withdrawals are likely to undermine economic efficiency. More specifically, these are drugs for which it is fairly widely believed that the injury risks are outweighed—from an economic efficiency perspective—by their health benefits. Limited product availability in this context refers either to an existing drug that—because of incentives stemming from the operation of the U.S. product-liability system—is either never marketed in the United States or had been on the U.S. market but was subsequently withdrawn. Collectively, the *amici* cite as examples Bendectin (a drug for severe morning sickness that was withdrawn from the U.S. market in 1983), various manufacturers withdrawing childhood vaccines from the market or exiting the U.S. vaccine market entirely prior to the adoption of the NCVIA in 1986, Norplant, and withdrawal in 1987 of the only vaccine available in the United States for Japanese encephalitis (Troy, 2007, p. 89). Thus, with the exception of Norplant, all of the offered examples date back to at least the 1980s.

What is the empirical evidence that product-liability exposure has caused manufacturers to withdraw pharmaceuticals from the U.S. market that made substantial contributions to public health? First, consider Bendectin, which is offered as an example in all four of the documents that discuss product withdrawals. The four documents cite on this score Lasagna (1991), but not Green (1996) and Sanders (1996), book-length studies of Bendectin. As discussed in Chapter Two, the confidence and nuance with which these three authors attribute Bendectin's withdrawal to product liability differ somewhat. It seems reasonable to accept the inference, however, that in the absence of product-liability exposure, Bendectin would have remained available in the United States. For example, both Green (1996) and Sanders (1996) studied the Bendectin saga in great depth, both provide considerable support for the inference, and neither disputes that product liability played an important role in greatly reducing Bendectin's profit prospects in the United States.

Second, consider vaccines, which are generally accepted within the medical community as having uncommonly large public health benefits.¹⁵ Troy (2007, p. 89)—citing only Lasagna (1991, p. 344)—reports that “the sole manufacturer of a vaccine to prevent Japanese encephalitis would no longer supply the product in the United States because of product liability.” Lasagna (1991, p. 344) relies on Marcus (1988) on this claim, and Marcus reports that the vaccine's manufacturer ceased U.S. clinical trials because it “did not have appropriate liability insur-

¹⁴ As emphasized in Chapter Two, the present monograph focuses on the economics of pharmaceutical product liability, and ignores, for example, issues related to fairness of compensation. Some of the *amici* supporting preemption dismiss the compensation function because of the notoriously high transaction costs of tort compared with other compensation mechanisms.

¹⁵ For example, IOM (2011, p. 4): “Vaccines offer the promise of protection against a variety of infectious diseases . . . [and] remain one of the greatest tools in the public-health arsenal.”

ance.” PhRMA (2007, p. 11) quotes Noah (2003, p. 392): “Tort litigation may drive from the market not only individual manufacturers of multi-source drugs but also entire product lines.” But Noah offers no additional empirical information supporting this claim, nor does he cite empirical studies that do.¹⁶ Regarding market exit by several vaccine manufacturers, PhRMA (2006, p. 12) cites Viscusi’s article (2000, p. 538), which states, “Liability hazards led many firms to exit the vaccine market.” But Viscusi provides no original evidence. In fact, however, both Congress of the United States, Office of Technology Assessment (1979) and IOM (1985) documented declining numbers of vaccine producers.¹⁷

Finally, consider Norplant. As described in Chapter Four, its manufacturer (Wyeth) quietly withdrew Norplant from the U.S. market without attributing this decision to product liability. But it would not be unreasonable to infer that Norplant’s product-liability problems left American women without access to a contraceptive that many knowledgeable observers viewed as safe, convenient, and effective. (See, for example, Birenbaum, 2001.)

Higher Drug Prices

Troy (2007), Calfee et al. (2008), and DRI (2008) argue that product-liability exposure tends to increase drug prices. A socially undesirable effect of higher prices would be reduced use of such a drug (according to the law of demand from basic microeconomics) and, as a result, lower health benefits from the drug. The only examples of liability-induced price increases offered by the preemption supporters are oral polio vaccine (OPV) and diphtheria, pertussis, tetanus (DPT) combination vaccine. Rapid price increases of these childhood vaccines date back to the late 1980s (Garber, 1993, Chapter 7; Manning, 1994) and were a major consideration in the adoption of the NCVIA.

What is the evidence that product liability increases drug prices? Regarding oral polio and DPT (as well as MMR, which *amici* do not cite) vaccines during the late 1980s, the evidence implicating product liability is fairly strong. Specifically, Garber (1993, pp. 105–110) provides evidence in graphical form and Manning (1994) provides econometric evidence that the prices of OPV, DPT, and MMR vaccines did increase dramatically during the mid- to late-1980s because of substantial (event-driven) increases in perceived liability exposure of vaccine manufacturers.¹⁸

Regarding prices of other drugs, as described in Chapter Two, Manning (1997) offers econometric evidence—based on comparing 1990 prices of 119 selected drugs in the United States and Canada—that higher U.S. drug prices due to U.S. product-liability exposure were not limited to childhood vaccines. However, this evidence is of questionable reliability because,

¹⁶ Noah (2003, fn. 85) does cite Garber (1993) “generally” on this possibility. Garber’s conclusions about this issue, however, are based on a mixture of theory and empirical information; in particular, Garber does not offer any direct empirical evidence about effects of product liability on withdrawals of products with wide support among medical professionals.

¹⁷ Apart from market withdrawals of particular vaccines and exits from the U.S. market of some vaccine producers, at different times there have been shortages of some vaccines, which can be viewed as a less extreme form of vaccine availability problems. Some vaccine shortages seem attributable to reduced numbers of suppliers, which, in part, seem attributable to product liability. Other factors contributing to limited U.S. vaccine supply (and shortages of other drugs) include delays in FDA approval and cost-containment efforts. See Noah (2003).

¹⁸ Garber (1993, pp. 118–119) argues on theoretical grounds that substantial effects of product liability on pharmaceutical prices are likely to be the exception, not the rule.

for example, of Manning's use of crude proxy variables to represent liability risk in the United States (see Chapter Two).¹⁹

Reduced Innovation

Troy (2007), PhRMA (2007), Calfee et al. (2008), and DRI (2008) argue that product-liability exposure has reduced the total amount of R&D aimed at developing (alternatively, inventing) new drugs or induced drug developers to shy away from efforts to develop drugs that are believed to be subject to unusually high levels of product-liability exposure and risk. Collectively, they cite contraceptives, an AIDS vaccine, other vaccines, and drugs for rare diseases (often called *orphan drugs*) as examples of products that were not developed because of liability concerns. To what extent are these claims supported by empirical evidence?

First, consider claims about particular kinds of pharmaceuticals that may not have been developed because of product liability. There cannot be direct empirical evidence of such effects because we cannot observe what would have happened in the absence of product liability. Nonetheless, Mastroianni, Donaldson, and Kane (1990) make a fairly persuasive (inferential) case that product-liability concerns have been an important factor in causing a substantial decline in efforts to develop new contraceptives. The more recent experience with Norplant in the United States is likely to have reinforced concerns of would-be contraceptive developers. Regarding the lack of an AIDS vaccine, the claim that product liability is a substantial factor dates back at least to 1992—see Troy (2007, p. 108, fn. 31)—but 20 years later, no AIDS vaccine was on the market despite considerable efforts to develop one. Regarding orphan drugs, it seems likely that even if product liability deters some product-development efforts, product-liability exposure is unlikely to tip the balance in many cases. This is because of the fairly small markets that are a defining characteristic of orphan drugs. Thus, it seems likely that there would typically be insufficient financial incentives to induce companies to invest in drug development even if there were no liability exposure.

Consider now what appears to be the only econometric evidence on effects of product liability on pharmaceutical innovation. In particular, Finkelstein (2003, 2004) focused on efforts to develop new vaccines. Troy (2007, p. 108, fn. 23) reports that Finkelstein (2003) finds that the institution of the Vaccine Injury Compensation Fund (VICF) created by the NCVIA of 1986 “led to a statistically significant increase in new clinical trials.” However, Finkelstein (2004)—the revised, published version of Finkelstein (2003)²⁰—states that “Most of the [R&D] investment induced by the VICF was probably . . . wasteful [business stealing]” (p. 555).²¹ Thus, the researcher who developed the only evidence cited by Troy (2007) to support the statement that “Expenditures on research and development increase when liability costs decrease” (Troy, 2007, p. 87) subsequently concluded that any additional R&D attributable to the VICP (which lessened liability exposure for selected vaccines) probably undermined

¹⁹ It seems likely that reasonable people would disagree about the reliability of Manning's conclusions.

²⁰ Finkelstein (2004, p. 546) refers to Finkelstein (2003) as “[t]he working paper version of” Finkelstein (2004).

²¹ Finkelstein uses the term *business stealing* to refer to R&D that affects the shares of vaccine sales of different drug companies but confers little, if any, social benefit and, thus, is “wasteful.” The quoted sentence alerts or reminds readers that sometimes the social benefits of innovation efforts fall short of their social costs. More specifically, in assessing the economic effects of product liability, we cannot safely presume that all increases in efforts to innovate are economically worthwhile from a societal point of view. Some innovative effort (or R&D spending) may be inefficient because, for example, companies competing to be the first to market a drug of a particular kind may engage in duplicative efforts.

economic efficiency. There appears to be no other direct empirical evidence about the effects of PPL on levels of effort to develop new drugs.²²

Inefficient Effects of Product Liability on Drug Safety

Maximizing the safety of drugs (or minimizing drug-related injuries or risks) is not a sensible policy goal. For example, we could minimize drug injuries by simply banning drugs altogether. From an economic perspective, the social goal is to achieve an economically efficient level of safety. Conceptually, the efficient level of safety is the level for which increments in safety involve equality of (marginal) social benefits and (marginal) social costs.²³ Several of the arguments of preemption supporters summarized in Table 5.1 pertain, in fact, to different aspects of the potential for FTW claims to affect drug safety in inefficient ways.

First, all five of the documents supporting preemption raise the issue of “overwarning.” Troy (2007, p. 91) argues that a result of holding companies liable for *failure-to-warn* is “creating an incentive for drug manufacturers to include warnings relating to all possible risks, even those that are trivial, extremely rare, or unproven.” The preemption supporters raise, collectively, two potential, socially undesirable effects of overwarning, namely, (1) deterring physicians from prescribing the best drug for a patient, due either to physicians not understanding the importance of the various warnings or overreacting to particular warnings, and (2) deterring patients who are aware of the warnings from filling their prescriptions or using the drug as much as prescribed (i.e., undermining patient compliance or adherence with prescribed therapies).

There appears to be no consensus in the medical community about the effects of extensive and detailed warnings on drug safety, but some medical researchers have expressed substantial concern. For example, drug labeling—which includes warnings and other information for prescribers—has been described as being “poorly organized; . . . stuffed with often irrelevant information; . . . may include an important fact about safety in any number of places . . . ; and . . . often fails to distinguish between a drug’s side effects and problems that may not even be causally related to its use” (Avorn and Shrank, 2006, p. 2409). Moreover, in its proposed rule about prescription drug labeling,²⁴ the FDA reports results from some focus groups with and surveys of physicians that provide additional evidence (U.S. Department of Health and Human Services, Food and Drug Administration, 2000, pp. 81083–81085). For example, the initial two physician focus groups (held in 1992) resulted in recommendations from physicians that they thought would help them find the information they often seek. These recommendations include “reducing or eliminating anecdotal, marginal information” (U.S. Department of

²² Garber (1993, Chapter 9) offered some indirect evidence on this score, however. He developed a simulation model calibrated using empirical information specific to drug markets and FDA drug regulation to explore the sensitivity of incentives to engage in clinical trials or to market an approved drug in the United States (namely, the expected present value of future profits, net of liability costs) to unusual levels of liability risk. He concluded, for example, “incentives to innovate can be very sensitive to liability uncertainty and risk” (p. 167). He also concluded, however, that such decreases in incentives would likely not affect, for example, efforts to develop (1) drugs for rare diseases because financial incentives to engage in R&D are usually insufficient even in the absence of any liability exposure or (2) drugs with especially high sales potential (so-called blockbuster drugs) because their profit potential often provides more than enough incentive to proceed with innovative efforts even in the face of unusually high liability risk.

²³ Stated differently, if achieving an increase in safety in a particular way requires higher social costs than the resulting social benefits, then that increase in safety is economically inefficient.

²⁴ This proposed rule led to U.S. Department of Health and Human Services, Food and Drug Administration (2006), the final rule that contained the preemption assertion.

Health and Human Services, Food and Drug Administration, 2000, p. 81084). Moreover, a subsequent survey of physicians led to the finding that “[p]hysicians believe that labeling overly stresses the occurrence of extremely rare events” (U.S. Department of Health and Human Services, Food and Drug Administration, 2000, p. 81084).

Recent empirical evidence suggests, however, that FDA efforts to reduce overwarning (through the new labeling rule that contained the preemption assertion) have not (yet) been very successful. Specifically, Duke, Friedlin, and Ryan (2011) analyzed drug labels as they existed in late 2009 and commented on their empirical findings as follows (p. 946) “the presence of . . . excess data still may induce information overload and reduce physician comprehension of important safety warnings. . . . This finding underscores the tremendous challenge faced by the FDA in reversing the long-standing trend toward overwarning.”^{25,26}

The second major safety-related argument of *amici* supporting preemption pertains to the possibility of inefficiently *high* safety levels. The argument is that increases in safety induced by product liability are likely to be inefficient because FDA safety standards are likely to be inefficiently high. Calfee et al. (2008, pp. 6–8) advance this argument, which is summarized in Table 5.1 related to the “excess caution [of the FDA] in drug approval.” More specifically, the argument²⁷ is that the FDA receives more criticism (including from Congress) for approving a drug that causes widespread injury than the FDA is criticized for failing to approve a drug that would have conferred large health benefits and relatively few injuries. The argument is theoretical, but plausible; there appears to be no empirical literature supporting or refuting it. Its plausibility is demonstrated by the fact that a committee of IOM (Baciu, Stratton, and Burke, 2007) shares the concern or finds the argument sufficiently plausible to highlight it. In particular, they write (p. 69):

Congressional concern about the public’s safety may be one contributing factor to what the industry and other critics have seen as the agency’s historically risk-averse stance in carrying out its regulatory duties. In their view, the agency has generally been more likely to err on the side of greater caution in approving drugs than to err on the side of faster approval, perhaps in response to the fact that congressional investigations generally focus on errors of commission (approving an unsafe drug) rather than omission (not approving a potentially good drug).

This argument, even if correct, is incomplete. Specifically, *amici* supporting preemption do not address the FDA’s ability to achieve their targeted levels of safety in a world of incomplete compliance preapproval²⁸ and possibly inadequate incentives for companies to continue to study a drug’s safety and effectiveness post-marketing. For example, Kessler and Vladeck (2008, p. 483) write, “the FDA views the preemption question through the prism of the ini-

²⁵ Garber (1993, Chapter 8) also expressed concerns that—due to the learned intermediary doctrine—pharmaceutical product liability also deters manufacturers from providing consumer-friendly warnings to patients. None of the *amici* raises this argument, however.

²⁶ *New England Journal of Medicine* Editors and Authors (2008, p. 32) appear to be correct when they claim that *amici* raising concerns about overwarning have not offered “any evidence that medical professionals would be better off with fewer warnings.” This does not mean, however, that no such evidence exists or that there is no problem.

²⁷ This argument goes back at least as far as Grabowski and Vernon (1983).

²⁸ For example, product labeling at the time of FDA approval for marketing may reflect failures of companies to provide complete and accurate information about results of animal and clinical studies.

tial approval process, and spends little time addressing its ability to monitor drug safety *post-approval*” [emphasis in the original].²⁹ And, like the FDA in viewing the preemption question, *amici* supporting preemption do not consider how the FDA’s inability to enforce all of its regulations might lead to substantial discrepancies between the FDA’s safety standards and the actual levels of safety achieved. If there are substantial discrepancies, with actual safety falling below the FDA’s standards, then PPL exposure may often induce safety increases that enhance economic efficiency rather than undermining it.

Potential Detrimental Economic Effects of Product Liability—Summary

The *amici* briefs, Troy (2007), documents they cite, and other literature raise concerns about several purported economic effects of PPL. Empirical support for particular concerns runs the gamut from essentially nothing to fairly compelling.

Regarding drug availability, it seems reasonable to attribute to product-liability exposure the withdrawals of Bendectin, some vaccines during the 1980s and 1990s, and Norplant. The fact that there are no more-recent apparent examples admits different interpretations. For example, it may be that no other drugs with substantial support of the medical profession have been withdrawn because of product liability other than Norplant in 2002; alternatively, there may be other instances in which less visible withdrawals attributable to product liability have occurred.

Regarding prices, there is strong evidence that sharp increases in the prices of the OPV, MMR, and DPT vaccines during the 1980s were attributable to rapid and large contemporaneous increases in product-liability exposure of vaccines. The reliability of evidence presented in Manning (1997) indicating effects of product-liability exposure on drugs other than childhood vaccines and drugs generally is equivocal.

Regarding innovation, it appears to be impossible to develop direct empirical evidence of effects of product-liability exposure on efforts to develop new pharmaceuticals. There is, however, a fairly strong basis from which to infer that product liability has been a major factor in discouraging efforts to develop new contraceptives. The only econometric study of effects of product liability on pharmaceutical innovation finessed the difficulties associated with directly measuring liability exposure by exploiting a natural experiment. In particular, the institution of the NCVIA of 1986 lowered liability exposure associated with selected vaccines, but Finkelstein (2004) concludes that induced increases in efforts to develop new vaccines more likely undermined than enhanced economic efficiency.

Regarding claims about inefficient effects of PPL on product safety, Troy (2007) and the *amici* in support of preemption emphasize two possibilities. First is the concern about overwarning and safety. There is no direct empirical evidence linking more extensive, complicated warnings to drug injuries. Focus groups and surveys of physicians conducted by the FDA in the early 1990s, however, provide some evidence that overwarning in drug labeling makes it more difficult for physicians to find and interpret the information they seek when they consult drug labels. Moreover, there is clear indication from medical literature that many in the medical community believe that overwarning is a serious concern. Second is the issue of the efficiency of the FDA’s safety standards and whether liability-induced increases in safety would

²⁹ Similarly, Garber (1993, pp. 125–132) argues that the FDA’s safety standards for approving drugs are likely to be inefficiently high, but he also argued that product liability is likely to increase drug safety in economically efficient ways by increasing company compliance with regulations, both before and after the FDA approves a drug for U.S. marketing.

undermine or promote economic efficiency. Preemption proponents argue for the former view. However, once incomplete compliance with the pertinent FDA regulations is considered—and the distinction between FDA *standards* (or targets) and *actual, achieved* safety levels is recognized—this theoretical line of argument opens up the possibility that liability-induced safety increases enhance economic efficiency.

Finally, it is somewhat surprising that Troy (2007) and the *amici* supporting preemption pay little attention to transaction costs of litigation. In particular, transaction costs of litigation are notoriously high in relation to the amounts of money paid in compensation, and the social costs of resources used up (or absorbed) in disputing are directly relevant to the economic efficiency of PPL.³⁰ Three caveats are in order, however. First, the empirical evidence in Kakalik and Pace (1986) pertains to all tort litigation and, thus, is not specific to PPL. Second, the extent to which the data used by Kakalik and Pace (1986) include mass torts is unclear, and the ratio of total transaction costs to total compensation paid could be very different for mass torts than for disputes that do not involve large numbers of similar cases. Third, the data used by Kakalik and Pace (1986) were from 1985, and it is not clear whether developments since then have tended to increase or decrease transaction costs, other things equal.

Economic Arguments Opposing Preemption

As detailed in Table 5.1, Kessler and Vladeck (2008) and the four *amici* briefs arguing against preemption claim that there are several socially desirable economic effects of pharmaceutical product-liability FTW claims. Broadly stated, the arguments emphasize that the FDA does not have sufficient resources to achieve their regulatory goals and that PPL is a socially valuable complement to FDA regulation. Specifically, these claims and their bases are as follows.

New Information About Side Effects of Particular Drugs

All five of the documents argue that product-liability FTW litigation—which commences after a drug is approved by the FDA—has in several instances resulted in discovery of information about side effects or injury risks that were previously unknown to the FDA.³¹ Kessler and Vladeck (2008, pp. 492–494)—who cite Kesselheim and Avorn (2007) and several reports in the popular press—offer the examples of Celebrex, Vioxx, olanzapine (Zyprexa), Halcion, Zomax, Paxil, and other antidepressant drugs. Members of Congress (2008, p. 28) use several of the same drugs as examples as well as Bextra, Avandia, Rezulin, and Baycol.

The empirical support for these examples appears to be sufficient to conclude that, at least in several instances, attorneys pressing pharmaceutical product-liability claims have uncovered important information bearing on product safety that the FDA did not possess. There is, however, no systematic empirical evidence concerning how common such examples are or the safety benefits (reductions in injuries) that have resulted from the discovery of such information.

³⁰ In contrast, compensation payments—whether appropriate or not—are not in themselves social costs because they represent “transfers” from one member of society (the defendant) to other members of society (claimants who receive the payments). Thus, the argument in PhRMA (2007, p. 9) that “Collectively these suits will cost individual companies billions of dollars” is not listed in Table 5.1 because it is not directly relevant to economic efficiency.

³¹ Similarly, Nagareda (2006, p. 5) argues that “tort litigation has served as an important means for the identification and dissemination of new information about product risk . . .”

Deterrence of Socially Undesirable Corporate Behavior

Carpenter et al. (2008, p. 17)—who also cite Kesselheim and Avorn (2007)—emphasize that product-liability litigation has also uncovered evidence of “questionable practices by manufacturers.” Examples of alleged practices—such as failing to report adverse events to the FDA, downplaying the extent or severity of side effects, failing to make clinical trial data public, and delaying public reports of adverse events—are discussed by Kesselheim and Avorn (2007). As suggested by Carpenter et al. (2008, pp. 7–8), California Medical Association (undated, p. 3), Members of Congress (2008, p. 28), and *New England Journal of Medicine* Editors and Authors (2008, p. 5), the potential for litigation to uncover inappropriate corporate behavior increases the potential costs of engaging in such behavior and thus, at least in theory, will tend to deter manufacturers from engaging in such practices.³²

The proposition that exposing such “questionable practices” reduces their future prevalence, however, is a theoretical proposition or hypothesis, albeit a plausible one. There appears to be no direct empirical support for this hypothesis, however. This is hardly surprising given the extreme difficulty, and, perhaps, virtual impossibility—see Chapter Two—of developing direct empirical evidence concerning how product-liability exposure affects corporate behavior.

Potential Desirable Economic Effects of Product Liability—Summary

There are several examples of instances in which product-liability litigation has uncovered important, safety-related information previously unknown to the FDA. In principle, this information could provide a basis for FDA actions to improve the safety with which particular drugs are used or to improve FDA policies more broadly. There appears to be no systematic, reliable empirical information about such FDA responses, however. There is also a substantial theoretical basis for expecting that exposing “questionable practices” by drug companies will deter some future instances of such practices; there is, however, no direct empirical information bearing on this hypothesis. Finally, it is somewhat surprising that preemption opponents do not draw more attention to the role of product liability in leading to withdrawal—with or without FDA intervention—of drugs that many in the medical community view as too dangerous in relation to their health benefits.

Preemption of Failure-to-Warn Claims for Generic Drugs

In June 2011, the U.S. Supreme Court decided that, unlike the law for branded drugs articulated in their ruling in *Wyeth v. Levine*, FTW claims brought against manufacturers of generic drugs are preempted by federal law. More specifically, in *Pliva, Inc., et al. v. Mensing*, which involved generic versions of the brand-name drug Reglan, a majority of the court found *conflict* preemption. In particular, the majority found that a conflict exists because FDA regulations require the labeling of a generic drug to be identical to that of the corresponding brand-name drug and, thus, it was “impossible” for the manufacturer to comply with both FDA regulations and state product-liability requirements requiring adequate warnings.

³² Manufacturers that fail to meet their duties to protect their customers from injury and are identified as such might also experience major costs associated with lost sales of the drug in question or even of other drugs due damage to their companies’ reputations.

The dissenting opinion (signed by four justices) argued that the decision in *Pliva, Inc., et al. v. Mensing* was problematic for several reasons. In particular, the dissenters argued that the decision was inconsistent with the court's ruling in *Wyeth v. Levine* and that the basis on which the majority found it impossible for the defendants to comply with both federal and state law was unpersuasive (in giving too much weight to what generic manufacturers may do without approval by the FDA) especially in light of precedent establishing a "presumption against pre-emption." The dissenters also argued that the decision "leads to so many absurd consequences" (dissent, p. 18) that it is very doubtful that Congress intended to preempt state FTW claims for generic drugs. Finally, all nine justices agreed that (at least from the point of view of the plaintiffs) "finding pre-emption here but not in *Wyeth* makes little sense" (decision p. 18; see also, dissent p. 2).

Whether this ruling leaves plaintiffs injured by generic drugs without any avenue to seek compensation is not clear, with the exception of claims brought under California law. Specifically, in November 2008 an appeals court in California found in *Conte v. Wyeth* that the manufacturer of the *branded version* can be held liable for injuries caused by a generic drug even when the generic was manufactured and sold by another company (Noah, 2010; Rostron, 2011).³³

Would Failure-to-Warn Litigation Pass a Social Cost-Benefit Test?

As just detailed, proponents and opponents of preemption of pharmaceutical FTW claims emphasize putative economic pros and cons of such litigation. The majority in *Wyeth v. Levine* did not find congressional intent to preempt in the case of branded drugs and accordingly ruled that such legal claims are not preempted. This legal outcome does not address a fundamental question concerning the economics of personal-injury PPL litigation, namely, would a preemption finding have enhanced economic efficiency? Stated differently, does PPL FTW litigation pass or fail a social cost-benefit test?

Sources of Confusion in the Preemption Debate

The debate over preemption can be difficult to put into perspective because of some distinctions that are sometimes blurred. First, the U.S. Supreme Court ruling in *Wyeth v. Levine* was based on legal, rather than economic, questions. Second is the distinction between effects of FTW litigation on economic outcomes determined before versus after FDA approval of a product. Preemption proponents emphasize the former and preemption opponents—along with Baciu, Stratton, and Burke (2007)—emphasize the latter.³⁴ Central, and contentious, issues related to this distinction are the appropriateness of product warnings at the time of FDA approval and how effectively and quickly warnings are modified as new information emerges from experience, including post-approval (or "phase IV") clinical trials and reports of adverse events experienced by individual patients. Third, it is important to distinguish between the FDA's

³³ In January 2009, the California Supreme Court decided not to review the lower-court ruling (Morgan Lewis, 2009).

³⁴ Similarly, in a brief discussion arguing that FDA regulation of pharmaceuticals greatly undermines the case for product liability, Polinsky and Shavell (2010, pp. 1450–1451) focus on preapproval regulation, and they address neither the potential roles of product liability after a drug is marketed in the United States nor the possibility that product-liability exposure increases compliance with regulations.

goals and the extent to which these goals are achieved in practice. Proponents of preemption rarely acknowledge that the FDA's enforcement capabilities are limited and that in principle (1) failure to comply with FDA regulations—for example, failure to accurately report adverse outcomes in clinical trials or update warnings based on information that emerges after the drug is marketed—can threaten public health and undermine economic efficiency, (2) product liability strengthens incentives to comply because evidence of failure to comply can be devastating for defendants,³⁵ and (3) sometimes, important safety information that would otherwise be unavailable to the FDA is unearthed by plaintiffs' attorneys through discovery in FTW lawsuits. Fourth, some of the disagreement among the arguments of preemption proponents and opponents reflects differences in social goals. In particular, some focus on promoting economic efficiency and others seek to increase product safety even if the social benefits of doing so may fall short of the social costs (in which case increases in safety undermine economic efficiency).

The Overall Economic Efficiency of FTW Litigation Is Unknown

Both proponents and opponents of preemption have cogent arguments and/or empirical evidence to support at least some of their claims about economics effects. Thus, it appears that there are both substantial social benefits and substantial social costs of FTW litigation. We cannot, however, compare the social benefits and costs quantitatively. More specifically, there is no reliable empirical basis for estimating in dollar terms the social costs or benefits of liability-induced lack of availability of products that promote public health, price increases, or effects on product safety, effectiveness, or innovation.

³⁵ See the discussion of RCDs in Chapter Three.

Incentives Stemming from Other Litigation Affecting Safety and Effectiveness

To this point, we have emphasized product-liability litigation brought on behalf of individuals alleging personal injuries caused by pharmaceuticals. Some of the decisions of pharmaceutical manufacturers that determine product safety and/or effectiveness discussed in Chapter Two and summarized in Table 2.1 are also likely, however, to be affected by other kinds of litigation. I refer to such litigation, which is the subject of this chapter, as being safety and effectiveness related (to personal-injury, product-liability litigation) or simply “related litigation” for brevity. As will become clear as we go along, the first three kinds of litigation considered in this chapter (and, perhaps, also the fourth) appear to have been much more frequently brought against pharmaceutical companies since 1990.

This chapter considers four kinds of related litigation brought against drug companies, namely:

- civil and criminal complaints brought by DOJ under the federal FDCA, the federal FCA, or both
- civil and criminal actions brought by state AGs under state CPAs and/or other causes of action
- civil actions alleging financial injury brought by private plaintiffs, often under state CPAs and/or other causes of action
- civil actions brought by stockholders of drug companies against the companies’ officers and directors alleging violations of federal securities laws or failure to satisfy their fiduciary duties to stockholders.

The allegations made in these complaints and lawsuits seem primarily to pertain to actions by pharmaceutical manufacturers after their products are approved for sale in the United States, and they most often involve product promotion.¹ More specifically, the alleged actions often include one or more of misrepresenting product risks, exaggerating product effectiveness, and promoting products for off-label use.

The remainder of this chapter is organized as follows. The next section describes and discusses actions brought by the DOJ. The section after that is a digression about CPAs and policy controversies pertaining more broadly than pharmaceuticals (because little analogous writing has focused on CPAs and pharmaceutical companies). The following two sections describe

¹ “Promotional labeling generally refers to everything *except* FDA-approved labeling” (Girard, 2009, p. 122; emphasis in the original).

and discuss use of CPAs by state AGs and private plaintiffs, respectively. Then we turn to shareholder suits. The penultimate section summarizes the chapter to that point and discusses whether and, if so, how pharmaceutical companies might change their behavior because of their exposure to litigation of the four types. The final section offers concluding remarks about these four kinds of related litigation.

Actions Brought by the U.S. Department of Justice

In recent years, the DOJ has filed civil and criminal complaints—and reached settlements—with several pharmaceutical companies alleging violations of the FDCA, the FCA, or both (Girard, 2009; Mello, Studdert, and Brennan, 2009; Almashat et al., 2010; Kesselheim, Studdert, and Mello, 2010).

As detailed by Girard (2009), allegations brought under the FDCA often involve “unlawful” promotion, which includes presentation of false or misleading information about safety and effectiveness for indications approved by the FDA, a pattern of promoting a drug for off-label use,² or both. Many actions brought against pharmaceutical manufacturers under the FCA³ are not relevant for our purposes because they seem unlikely to affect incentives for companies to provide more accurate and complete information about product safety and effectiveness or any other actions that could substantially affect product safety and effectiveness.

The FCA, which was enacted during the Civil War, pertains to fraud on the United States government.⁴ In the pharmaceuticals context, allegations under the FCA can involve any fraudulent actions that cause public health insurance programs, such as Medicare and Medicaid, and health care provided by the Veterans Administration, to pay more for pharmaceuticals than they would absent the alleged fraud.

Almashat et al. (2010) examine civil and criminal settlements or penalties paid by pharmaceutical companies to the federal or state governments from 1991 through November 1, 2010. They report, for example, that criminal and civil settlements paid by pharmaceutical companies (involving all types of allegations) had increased substantially over the previous 20 years; unlawful promotion allegations were among the most common allegations both in terms of numbers of DOJ actions and aggregate amounts of settlements; and *qui tam* (whistleblower)⁵

² Mello, Studdert, and Brennan (2009, Table 2, pp. 1562–1563) describe in tabular form ten enforcement actions alleging off-label promotion by pharmaceutical companies brought by federal or state authorities that resulted in settlements during the period 2004–2009. Their descriptions of the types of prescribing encouraged by the alleged off-label promotion (e.g., unapproved medical conditions or patient groups such as children) and the alleged methods of promotion are suggestive of the variety of circumstances involved in these enforcement actions.

³ Such as overcharging or paying kickbacks to purchasers and collusive behavior. For example, of the seventeen *qui tam* actions against drug manufacturers studied by Kesselheim, Studdert, and Mello (2010, Table 1, p. 1833) eight involved some form of overcharging and eight others involved allegations of off-label promotion.

⁴ Several states have their own false claims laws, including laws focused on Medicaid fraud (Almashat et al., 2010, pp. 5–6).

⁵ The *qui tam* provisions of the FCA are described by Kesselheim, Studdert, and Mello (2010, pp. 1832–1834) and, to a lesser extent, Girard (2009, p. 139). The account in this footnote relies on those sources. In a *qui tam* action under the FCA, private individuals (*whistleblowers* or *qui tam plaintiffs*) who have evidence of a violation may file confidential (*under seal*) complaints in federal court on behalf of the United States, and they may share in any eventual recovery. Once a *qui tam* complaint is filed, the DOJ investigates and may choose to take the lead in pursuing it. Girard (2009, p. 139) reports that the DOJ takes on the cases that are “most likely to succeed.” Shares of the recovery for all whistleblowers in a particular

actions became especially prominent since 2001, accounting for two-thirds of the total payments of pharmaceutical companies during that period.⁶ Large settlements—for example, of \$500 million or more—were not uncommon⁷ and seem likely to be due in part to very substantial risks associated with a felony conviction under either the FDCA or the FCA, including (see Girard, 2009, pp. 128, 136) exclusion from participation in government health programs for at least five years.^{8,9}

It is unclear, and controversial, why this kind of litigation against drug companies and the sizes of settlements have grown so much in recent years and whether this growth is socially desirable. More specifically, Almashat et al. (2010, p. 22) suggest that the upward trends in the number and size of government settlements with pharmaceutical companies are due in part to an upward trend in violations, argue that the penalties are too small relative to corporate profits to deter illegal behavior, and advocate larger penalties.¹⁰ In contrast, Girard (2009) argues against continued use of the FCA for several reasons, including lack of judicial review of DOJ theories and procedures, lack of DOJ concern about public health goals, and reliance on a dubious theory linking promotion to prescribing behavior (and, thus, effects on government costs).

State Consumer Protection Acts—Background and Controversies

Both state attorneys general and private entities have brought legal actions against pharmaceutical companies under state CPAs and/or other causes of action. Many of these lawsuits

case range from 15 to 25 percent, with the government determining the share (Kesselheim, Studdert, and Mello, 2010, p. 1834). Among 26 whistleblowers in FCA actions interviewed by Kesselheim, Studdert, and Mello (2010), for example, the amounts they received (net of attorney fees and taxes) were less than \$1 million for five of them and \$5 million or more for seven.

⁶ Girard (2009, p. 139) discusses how the DOJ employs information supplied by *qui tam* plaintiffs.

⁷ Specifically, according to Almashat et al. (2010, Table 3, p. 16), among the 20 largest settlements with pharmaceutical companies during the 20-year period are several involving allegations of unlawful promotion—for example, \$1.4 billion in 2009 (Zyprexa), \$601 million in 2007 (OxyContin), and \$600 million in 2010 (Botox)—and others alleging unlawful promotion along with other illegal activities—for example, \$2.3 billion in 2009 (Bextra and three other products), \$704 million in 2005 (Serostim), \$520 million in 2010 (Seroquel), and \$515 million in 2007 (Abilify and Serzone). Moreover, since the end of the time period studied by Almashat et al. (2010)—namely, November 1, 2010—there have been at least two more relevant DOJ actions in which settlements exceeding \$1 billion were pending as of late 2011. In particular, (1) Abbott Laboratories recorded an accounting charge of \$1.5 billion for the third quarter of 2011 to account for a potential settlement of charges that it promoted Depakote for off-label uses (Loftus, 2011) and (2) in November 2011, GlaxoSmith-Kline announced a \$3 billion “agreement in principle” to settle DOJ investigations into off-label marketing of nine drugs, including Avandia, Paxil, and Wellbutrin as well as overcharging of state Medicaid programs (Wilson, 2011; Raymond, 2011b). Girard (2009) provides more information about several of the cases reported in Almashat et al. (2010) and other cases settled for less than \$500 million.

⁸ Moreover, pressure to settle, even for very large sums, can be further strengthened by the possibility of corporate executives being held criminally liable as individuals under the “responsible corporate officer doctrine” (O’Connell and Rothfeld, 2011).

⁹ To foreshadow, the existence of such large settlements suggests that the financial incentives to avoid DOJ action can be large enough to affect corporate decisions that affect safety and/or effectiveness. See the discussion in the penultimate section of this chapter.

¹⁰ Another contributing factor is likely to be the increased use of *qui tam* actions since 2001 that is reported in Almashat et al. (2010).

relate to product safety and effectiveness. This section provides background about use of state CPAs generally. This digression is offered because there is little analogous literature focused on pharmaceuticals, and the issues raised in more general discussions appear to pertain to pharmaceuticals.

Many states have adopted CPAs that are patterned after the Federal Trade Commission (FTC) Act of 1914 (Schwartz and Silverman, 2005). Such laws are also referred to as “unfair competition laws,” “unfair trade practices laws,” “deceptive trade practices acts,” and “mini-FTC acts.” Unlike the case with the federal statute, almost all states allow private parties to bring claims under these acts.¹¹ Lawsuits brought under these laws—often alleging unfair trade practices or unfair competition—typically involve claims for financial, rather than personal, injury (Leghorn, Allen, and Brewington, 2006, p. 519; Schwartz and Silverman, 2005; American Tort Reform Foundation, 2006). These laws, and especially the private rights of action, are controversial.

Largely critical or cautionary accounts and analyses of the use of state CPAs include Center for Legal Policy at the Manhattan Institute (2002), Schwartz and Silverman (2005), Greve (2005), American Tort Reform Foundation (2006), Copland and Joyce (2006), Fisher (2007), and Searle Civil Justice Institute (2009).¹² Major criticisms of the recent use of these laws are well summarized by the following:

The broad wording of these statutes, the hope that they will be construed liberally in favor of the consumer, and a dearth of case law make these open-ended statutes especially attractive to plaintiffs’ lawyers who seek to circumvent traditional, rational requirements of the common law. . . . A few judges have turned CPAs into springboards for a “universal tort,” providing a claim in any lawsuit involving conduct that could possibly be categorized as unfair or deceptive. Claims that would traditionally have been brought as product liability, environmental, or contract claims are recast as violations of a consumer protection law and circumvent otherwise applicable and well-reasoned legal safeguards (Schwartz and Silverman, 2005, pp. 3–4).

The potential for suits to be brought as class actions—which are explicitly allowed by the CPAs of at least 14 states (Schwartz and Silverman, 2005, p. 29)—is particularly troubling to critics of CPAs (e.g., American Tort Reform Foundation, 2006, pp. 17–19; Center for Legal Policy at the Manhattan Institute, 2002, p. 11). Leading concerns are that (1) class actions may be viable under state CPAs that would not be viable as common-law product-liability suits, and (2) the financial stakes and risks posed by class actions can be so large that defendants may settle lawsuits even if they lack merit.¹³

Plaintiffs’ representatives have also raised concerns about CPAs being misapplied to the benefit of defendants. For example, according to Elizabeth Cabraser, a leading plaintiffs’ attorney:

¹¹ According to Leghorn, Allen, and Brewington (2006, p. 519), 49 states have at least one CPA with a private right of action; the exception is Iowa.

¹² Most of the critiques focus on legal issues and fairness concerns, rather than deterrence or economic effects. An exception is Greve (2005).

¹³ Certification of multistate or nationwide CPA classes is generally not possible because, for example, the statutes vary considerably across states (Zimmerman, 2006, p. 16-4.)

One thing that frustrates us on the plaintiff side as well is that notwithstanding what we think is the clear statutory language in most states . . . judges, who have been schooled in the common law, repeatedly—and intuitively, to some extent—reimport requirements of reliance, for example, into the consumer statutes (Center for Legal Policy at the Manhattan Institute, 2002, p. 44).¹⁴

Many have expressed concern about widespread use of CPAs in instances in which traditional product-liability claims are not viable. During the mid-2000s, however, this concern appears to have been more about potential future problems than instances of plaintiffs' successes. In particular,

Such lawsuits . . . appear to be product liability claims where lawyers would have difficulty showing that the product is unreasonably dangerous, that it caused any injury, or resulted in any loss to the plaintiff . . . thus far, courts appear to have kept their collective finger in this dam (Schwartz and Silverman, 2005, p. 64).

American Tort Reform Foundation (2006, p. 20) stated that it was likely that the prevalence of CPA suits would grow rapidly:

Although private actions under state consumer protection laws have been available for over 25 years, plaintiffs' lawyers and interest groups have only recently discovered their extraordinary potential for generating massive lawsuits and regulating entire industries. Now that the cat is out of the bag, state courts and legislatures must prevent lawsuit abuse.

In addition, a leading product-liability defendants' lawyer, Sheila Birnbaum, has reported:

It is rare today that I see a complaint that doesn't contain a deceptive trade practices and unfair competition count . . . a transformation is occurring away from breach of contract and fraud, which are hard to prove, and toward deceptive trade practice litigation, which is easy to prove (Center for Legal Policy at the Manhattan Institute, 2002, p. 7).

For purposes of the present study, the central question is how actual and potential litigation under CPAs affects the decisions of pharmaceutical companies that, in turn, affect economic outcomes described in Chapter Two. As with actions brought by the DOJ, litigation brought against pharmaceutical companies under state CPAs may or may not be relevant for our purposes. Litigation alleging, for example, overcharging or anticompetitive conduct are largely irrelevant for this study, because such litigation is unlikely to substantially affect company decisions determining the safety and/or effectiveness of particular drugs.

We now proceed to consider litigation brought under state laws—alleging violation of CPAs as well as other laws or regulations—that could affect manufacturer decisions relevant to product safety and effectiveness. We first discuss litigation brought by state AGs and then consider financial-injury litigation brought by private entities.

¹⁴ *Reliance* is a legal term that in the present context connotes that the plaintiff(s) depended upon or acted on the basis of (allegedly) misleading or deceptive information.

Safety- and Effectiveness-Related Litigation Brought by State Attorneys General

Use of state CPAs by state AGs appears to be considerably less controversial than litigation brought by private plaintiffs under the same laws. For example, Schwartz and Silverman (2005, p. 3)—who express substantial concern about the latter throughout that article—write in their Introduction that “The crucial difference between the [federal] FTC Act and CPAs is that most state laws, unlike the federal law, provide consumers with private rights of action. Unlike government agencies, private plaintiffs are not constricted to bringing actions in the public interest.”¹⁵

During the past decade, several pharmaceutical companies have settled claims brought by state AGs related to allegations of FTW, off-label promotion, and other forms of improper product promotion. For example,

- In January 2007, Bayer agreed to pay \$8 million to settle lawsuits brought by AGs in 30 states that alleged failure to adequately warn patients about Baycol’s risks (Lovering, 2007).
- Eli Lilly and Company has entered into several settlements involving Zyprexa: (1) \$1.42 billion settlement in 2009 with the DOJ and the Medicaid Fraud Control Units of 36 states for off-label marketing,¹⁶ (2) a \$62 million settlement in 2008 with 32 states and the District of Columbia brought under the CPAs of those states,¹⁷ and (3) settlements in 2008 and 2009 of claims brought by 13 states alleging personal injury and improper promotion totaling \$245 million (Eli Lilly and Company, 2011).
- In 2004, GlaxoSmithKline agreed to pay \$2.5 million (and agreed to provide information about clinical trials on its website) to settle a fraud lawsuit filed by the New York state AG alleging that the company concealed information about suicide risks of Paxil for children and teenagers (*APLR*, 2004).
- In 2007, Purdue Pharma agreed to pay \$19.5 million to settle claims of 26 states and the District of Columbia concerning promotion of OxyContin for more frequent use than approved by the FDA (*Wall Street Journal*, 2007).
- In 2008, Merck paid \$58 million to settle claims from 28 states and the District of Columbia alleging that the company “misrepresented the safety and improperly concealed the increased risks of Vioxx” (Kingsbury, 2008).
- In 2008, Pfizer settled for \$60 million suits brought by AGs in 33 states and the District of Columbia alleging improper promotion of Bextra (Koppel, 2008).
- In March 2011, AstraZeneca agreed to pay \$68.5 million to 37 states and the District of Columbia to settle claims involving deceptive marketing of Seroquel (Berkrot and Stempel, 2011).

¹⁵ Vairo (2011) reports that while actions by state AGs are not brought as class or mass actions, some courts have ruled that they are removable to federal court under the U.S. Class Action Fairness Act of 2005. She reviews recent case law on this question.

¹⁶ See Russell (2009) and DOJ (2009) for more information about the allegations and settlement.

¹⁷ See Berenson (2008) for more information.

- In August 2010, InterMune agreed to pay almost \$37 million to several states and the U.S. government to settle claims that the company promoted Actimmune for off-label uses (Loria, 2010).
- In October 2010, a jury delivered a \$258 million verdict against Janssen Pharmaceuticals in a case brought by the Louisiana AG alleging that the company misrepresented side effects of Risperdal (O'Brien, 2010b).
- In March 2011, Alpharma agreed to pay \$19.5 million to settle claims by several states alleging “misrepresentation of the safety and efficacy” of Kadian (O'Brien, 2010a).
- In June 2011, after a two-week trial, Ortho-McNeil-Janssen Pharmaceuticals was ordered to pay \$327 million for violating South Carolina’s consumer protection laws by deceptive marketing of Risperdal (Feeley and Church, 2011).

Moreover, several similar lawsuits were pending in mid-2011. For example,

- As of the end of 2010, Merck was facing 21 lawsuits filed by government entities, including the AGs of 13 states alleging that the company had “misrepresented the safety of Vioxx” (Merck & Co., Inc., 2011, p. 39).
- Seven states did not settle their suits with AstraZeneca when 37 states and the District of Columbia settled their Seroquel suits described above (Berkrot and Stempel, 2011).
- The AGs of Louisiana and Utah have filed suits “asserting various statutory and common law claims relating to . . . development and marketing of Avandia” (GlaxoSmithKline, 2011, p. 182).
- AGs of about 40 states “have indicated a potential interests in pursuing” litigation “relating to the promotion of RISPERDAL” (Johnson & Johnson, 2011, p. 64).

Safety- and Effectiveness-Related Financial-Injury Litigation Brought by Private Parties

Litigation alleging financial injury due to misrepresentation of safety or effectiveness of prescription pharmaceuticals has also been brought by private plaintiffs under state CPAs, other causes of action, or both. These include suits brought by third-party payers (TPPs) such as health maintenance organizations, health insurers, and labor unions. In many instances, these lawsuits allege violation of state CPAs,¹⁸ other legal theories, or both and are brought as class actions.

Perhaps the most prominent instance of a filed class action of relevance to our inquiry is the lawsuit brought against Merck in 2003 in New Jersey state court by International Union of Operating Engineers Local 68 Welfare Fund alleging financial injury to TPPs due to deceptive marketing of Vioxx. The history of the case through September 2007 is summarized by Voreacos (2007), upon which the account here is based. The case was brought under New Jersey’s Consumer Fraud Act as a national class action representing TPPs for pharmaceuticals. The trial court certified the class in 2005 and an appeals court upheld the certification. In September 2007, however, the New Jersey Supreme Court ruled that class certification was not

¹⁸ Schwartz and Silverman (2005, p. 31, fn. 160) report that “About two-thirds of CPAs specifically exempt acts or transactions regulated by, authorized by, or in compliance with rules and regulations of a federal or state government agency.”

appropriate. Thus, different payers would have to sue separately. According to Merck & Co. (2010, p. 38), a total of roughly 190 TPPs brought claims in New Jersey, and on September 15, 2009, Merck entered into an agreement to settle all of these claims for a total of \$80 million.

Another prominent legal battle involving a filed nationwide class action was brought in federal court in the Eastern District of New York and involved allegations that Eli Lilly “inadequately tested for and about side effects of Zyprexa and improperly promoted the drug” (Eli Lilly and Company, 2010, p. 33). In September 2008, a class of TPPs was certified that involved allegations of violation of the Racketeer Influenced and Corrupt Organizations Act (RICO), but the district judge declined to certify a class of individual payers or a class based on alleged violations of state CPAs (Mullenix, 2010). In September 2010, the class certification ruling was reversed by the U.S. Court of Appeals for the Second Circuit (Eli Lilly and Company, 2010, p. 33; Mullenix, 2010), and “[p]laintiffs are seeking review of this decision by the U.S. Supreme Court” (Eli Lilly and Company, 2010, p. 33).

A third prominent TPP case, brought by TPPs Kaiser Foundation Health Plan and Kaiser Foundation Hospitals in federal court in Massachusetts, involves allegations of off-label promotion of Neurontin by Pfizer. The lawsuit alleges violations of RICO and California’s Unfair Trade Practices law (Pfizer Inc., 2011a, p. 105). In March 2010, a jury returned a verdict for the plaintiffs which—after trebling damages under RICO—amounted to more than \$140 million (Van Voris and Lawrence, 2010). This verdict was entered by the trial judge in January 2011, and the defendant stated that it intended to appeal (Pfizer Inc., 2011a, p. 105).

There has also been a settlement of a lawsuit filed against GlaxoSmithKline in the U.S. District Court for the District of Minnesota for \$40 million with a class of roughly 42,000 health plans that paid for (off-label) Paxil use by children and adolescents (Marcotty, 2008; Whalen, 2008). Moreover, in 2006 GlaxoSmithKline agreed to settle a \$63.8 million class-action lawsuit involving individual purchasers of Paxil that also alleged off-label marketing to children and adolescents (Associated Press, 2006), which was subsequently renegotiated (Associated Press, 2007b).

It also appears that many other private claims for financial injury alleging misrepresentation of product safety or effectiveness or alleging off-label marketing are pending at the time this monograph was written. For example:

- A lawsuit similar to the Paxil case settled by GlaxoSmithKline in Minnesota in 2008 is pending in the same U.S. district court, in this instance “on behalf of all federal, state and local government entities that paid for prescriptions of Paxil to minors” (GlaxoSmithKline, 2011, p. 183).
- In 2010, Health Care Services Corp (HCSC) filed lawsuits against Pfizer on behalf of “itself and its affiliates, Blue Cross and Blue Shield plans” in four states involving allegations of “deceptive marketing activities including off-label promotion” of Celebrex and Bextra, and HCSC subsequently filed similar claims involving Geodon, Lyrica, and Zyvox (Pfizer Inc., 2011a, p. 104).

Shareholder Suits Pertaining to Pharmaceutical Safety and Effectiveness

Securities class actions (SCAs) allege financial injury from violations of the federal Securities Act of 1933 and Securities and Exchange Act of 1934.¹⁹ SCAs are brought in federal courts on behalf of groups of shareholders, usually for monetary damages. Broadly, these lawsuits allege that the defendant company failed to disclose information to investors. The general legal standard determining whether information must be disclosed to investors is whether the information is *material*. This standard was described by the U.S. Supreme Court in March 2011 as follows, “this materiality requirement is satisfied when there is a substantial likelihood that the disclosure of the omitted fact would have been viewed by the reasonable investor as having significantly altered the ‘total mix’ of information made available” (*Matrixx Initiatives, Inc., et al. v. Siracusano et al.*, p. 10).²⁰

Shareholder derivative suits (SDSs) are filed, usually in state courts, by a shareholder on behalf of a corporation (the corporation receives any monetary recovery) against officers or directors alleging that they violated a duty to the stockholders.²¹ These legal actions hold corporate officers and directors personally liable for failing to satisfy their duties to stockholders. There are two kinds of fiduciary duties under the law: (1) “the duty of care, which requires the exercise of reasonable skill, diligence and care in taking (or refraining to take) board action” and (2) “the duty of loyalty, which requires fairness (or disclosure and approval by either disinterested board members or shareholders) in self-interested transactions” (Romano, 1991, p. 56).

As with the other kinds of litigation discussed to this point, the SCAs and SDSs of interest are those that make allegations related to the safety or effectiveness of a particular drug or, in some instances, multiple drugs sold by the same company. A review of a sample of such lawsuits described in company reports to the SEC and litigation reporters suggests that most, and perhaps almost all, of the relevant allegations in particular claims fall into one or both of two categories, namely, failure to disclose (1) health risks of drugs and (2) how drugs were promoted, involving deceptive promotional messages, promotion for off-label indications, or both.²²

¹⁹ There are several causes of action for SCAs in the two statutes (e.g., under secs. 11 and 12 of the *Securities Act of 1933* and section 10B of the *Securities and Exchange Act of 1934*). It appears that many, and perhaps most, SCAs allege violations of the antifraud provisions of sec. 10b of the *Securities and Exchange Act of 1934* and the SEC’s Rule 10b-5 that implements this section. I am aware of no studies quantifying the relative frequencies of SCAs invoking different causes of action generally or for pharmaceutical companies. For an overview of provisions of the *Securities Act of 1933* and the *Securities and Exchange Act of 1934*—including the several causes of action available to private parties (rather than the SEC)—see Legal Information Institute (undated[a] and [b]).

²⁰ Cornerstone Research (undated) indicates that SCAs brought against pharmaceutical companies are not uncommon. For example, they report that “144 [securities] class actions were filed against 126 pharmaceutical companies between 2002 and 2009, including 15 of the 22 pharmaceutical companies included in the S&P 500 in 2009.” Not all of these SCAs are relevant to the present inquiry, however. Cornerstone reports counts of SCAs separately for four categories, namely, “issues in clinical trials, issues with drugs on the market, accounting issues, and regulatory approval issues.” It seems that SCAs of interest in this monograph would fall into one or both of the first two categories, which account for 79 of the 144 SCAs (Cornerstone Research, undated, Figure 2).

²¹ Such lawsuits can be viable only if the corporation had a valid cause of action but failed to act.

²² Another type of allegation, which seems less common, involves disclosure of eventual litigation costs. For example, in 2008, Bayer settled for \$18.5 million an SCA alleging, among other things, that the company misled stockholders about the potential financial liability associated with Baycol (Bayer Corporation, 2008, p. 188; 2009, p. 231).

Examples of lawsuits in the first category (disclosures about health risks of drugs) include the following:

- Several SCAs and SDSs alleging that Merck failed to disclose risks of Vioxx, which had been consolidated in a federal MDL, were dismissed by the MDL judge in 2006 and 2007 (*APLR*, 2006; *ADRLR*, 2007). Both of these dismissals, however, were overturned by the U.S. Court of Appeals for the 3rd Circuit (Associated Press, 2007a; Barris 2008).²³ As of the end of 2010, the consolidated suits were pending in the MDL in New Jersey (Merck & Co., 2011, p. 126).
- Beginning in 2004, SCAs were filed against Pfizer, Pharmacia, and selected former and current directors and officers of these companies alleging, among other things, violations of “federal securities laws by misrepresenting the safety of Celebrex and Bextra” (Pfizer Inc., 2011a, p. 103).
- An SCA was filed against AMAG Pharmaceuticals in 2010 alleging that, prior to its initial public offering, AMAG failed to disclose adverse reactions associated with the drug Feraheme (*Boston.citybizlist.com*, 2010); the suit was dismissed in August 2011 (Palmer, 2011).

Examples of lawsuits in the second category (disclosures about how drugs were promoted) include the following:

- SDSs filed in various courts since September 2009 alleged that current and former Pfizer officers and directors “breached fiduciary duties by, among other things, causing or allowing Pfizer to engage in off-label promotion of certain drugs, including Bextra.” In November 2009, the federal cases were consolidated in an MDL—*In re Pfizer Inc. Shareholder Derivative Litigation*. A settlement of the federal cases received preliminary approval in December 2010. The settlement includes \$75 million from directors and officers insurers to pay the “plaintiffs’ legal fees and expenses” and to fund a “new Regulatory and Compliance Committee of the Board of Directors” that will be created as part of the settlement (Pfizer Inc., 2011a, p. 104).
- As of the end of 2009, Eli Lilly had seven SDSs filed against current and past directors and officers since January 2008 alleging “improper marketing of Zyprexa, and in certain suits, Evista and Prozac” (Eli Lilly and Company, 2010, pp. 15–16).
- As of the end of 2010, Johnson & Johnson had seven SDSs pending in U.S. District Court for the District of New Jersey that were consolidated in August 2010 and another SDS in a New Jersey state court. These lawsuits have similar claims including “improper off-label marketing of pharmaceutical . . . products” (Johnson & Johnson, 2011, pp. 68–69).

²³ The SCAs were dismissed on the grounds that the two-year statute of limitations specified under federal law had run its course before the lawsuits were filed. The controversy centered on when the limitations period began. The issue was resolved by the U.S. Supreme Court in its decision on April 27, 2010, in *Merck & Co. Inc. et al. v. Reynolds et al.* affirming the ruling of the 3rd Circuit that the suits were, in fact, timely (Mauro, 2010).

Summing Up

Chapters Four and Five considered the economics of personal-injury product-liability litigation against pharmaceutical companies. The current chapter considered other kinds of litigation related to drug safety and/or effectiveness that are in this sense related to PPL. The chapter provides examples of lawsuits resolutions that have been sufficiently costly to drug companies to suggest that at least some of these forms of related litigation—alone or in conjunction with other kinds of litigation that penalize the same or similar company behavior—could affect future behavior and thereby the future safety and effectiveness of prescription drugs.

Are corporate decisionmakers likely to perceive sufficient financial threats from the types of litigation considered in the chapter to affect their behavior? If so, what kinds of behavior are likely to be affected? The answers to these questions appear to differ across the four kinds of related litigation; consider them in turn.

Litigation brought by the DOJ against pharmaceutical companies—much of it alleging (illegal) off-label promotion and/or deceptive marketing—has resulted in several settlements of \$500 million or more, with at least a few settlements exceeding \$1 billion. Such litigation will tend to discourage behavior that DOJ investigates and sanctions. Many of the settlements have received substantial publicity in the popular and trade press, and it is likely that most—and perhaps virtually all—relevant drug company decisionmakers have taken note. Moreover, it appears that since 1990 the frequency of DOJ claims alleging off-label promotion and deceptive marketing and the sizes of resulting settlements have increased substantially. These developments suggest that drug company decisionmakers have revised their beliefs over the past 20 years or so about their potential exposure to such litigation by, for example, increasing their assessments of the (1) probability of DOJ action if a company does engage in a pattern of off-label promotion or deceptive marketing, (2) probability that such a DOJ action would result in a settlement, and (3) sizes of potential settlements. Nonetheless, it is not clear how often companies' potential financial exposure—by itself—would be enough to induce them to refrain from off-label promotion or deter them from deceptive marketing. More specifically, back-of-the-envelope calculations suggest that potential DOJ actions alone would deter future off-label promotion under only some circumstances despite the potential for settlements exceeding a billion dollars. This is because the financial benefits of off-label promotion to a drug company might, in some instances, be even larger than the company's expected costs of DOJ actions.²⁴

²⁴ Consider a simple, hypothetical example that illustrates the tradeoffs involved and suggests that under some circumstances exposure to a future DOJ action alone might not deter all off-label or deceptive promotion. Suppose that a drug company's decisionmakers are considering whether to promote Drug A in a particular way that exposes them to DOJ action. The company's financial upside of this (at least arguably) off-label or deceptive promotion would be the incremental profits from Drug A due to the incremental sales attributable to the promotional actions under consideration. The financial downside would include costs of the additional promotional actions, legal costs if the DOJ investigates, and potential payment to settle a DOJ action. (There are other factors that would tend to discourage the promotional activities, such as the expected costs in other kinds of litigation, potential loss of company reputation, and criminal sanctions as well as the strength of the corporate culture promoting honesty and regulatory compliance.) Suppose—hypothetically and somewhat arbitrarily—that the decisionmakers believe that (i) the promotional activities under consideration would increase operating profits from Drug A (net of the costs of these activities) by \$X million; (ii) if they undertake this promotion, there would be a 50 percent chance of a DOJ investigation, a 90 percent chance that the investigation would lead to a settlement, and if there is a settlement, it would be for \$1 billion; and (iii) if there is an investigation, the company will incur legal costs of \$20 million. Then, according to (ii) and (iii), if the company chooses to undertake the promotional actions, their mathematically expected legal costs plus payment to the government would be \$460 million—i.e., $(0.5)(\$20 \text{ million}) + (0.5)(0.9)(\$1 \text{ billion})$. Then, ignoring discounting to present value, the possibility of a DOJ investigation alone (that is, ignoring the other disincentives

Several actions brought by state AGs under state CPAs and other causes of action have been settled for tens of millions of dollars—far less than the largest settlements with the DOJ. There have also been two jury verdicts of roughly \$250 million and \$325 million. Many of the drugs involved in these actions have also been the targets of mass tort attempts by plaintiffs' attorneys (e.g., Avandia, Baycol, Bextra, OxyContin, Vioxx, and Zyprexa). The central allegations in many of the state AG suits—namely, off-label promotion and different activities alleged to misrepresent product risks and effectiveness—are different from those in the personal-injury mass torts—namely, injury causation and whether warnings were legally adequate. Thus, as is the case with the DOJ actions, much of the activity of state AGs is likely to affect different decisions than does exposure to personal-injury litigation. Finally, many of the state AG suits—such as those alleging off-label promotion—are likely to fortify deterrence effects of DOJ actions.

It is even more difficult to gauge the financial threat perceived by drug company decisionmakers from private lawsuits brought under state CPAs and other causes of action. Many of these financial-injury lawsuits allege that institutional or individual purchasers of particular drugs would not have paid as much as they did pay were it not for illegal or deceptive behavior by drug companies. More specifically, the private lawsuits have involved a variety of allegations including off-label promotion and misleading purchasers about drug safety and/or effectiveness in different ways. Prominent lawsuits brought by TPPs have involved legal battles over certification of class actions, with some instances of trial courts certifying and appeals courts overturning class certification. A key unknown about the future financial threats to drug companies—and the likelihood that these threats will alter future company behavior—is the extent to which financial-injury class actions will be certified. For example, while Merck paid a total of \$80 million to settle 190 separate TPP lawsuits filed in New Jersey after the plaintiffs failed to gain class certification, this settlement amounts to less than \$500,000 per TPP. If class-action certification is viewed as unlikely for future lawsuits, it is possible that recoveries of this approximate size will not suffice to induce TPPs to file similar lawsuits in the future. Finally, to the extent that private lawsuits are costly to drug companies and allege the same kinds of behavior as DOJ and state AG actions, they should be expected to fortify, to at least a minor degree, incentives of drug companies to avoid engaging in off-label promotion and deceptive marketing.

The fourth type of litigation considered in this chapter comprises lawsuits brought by drug companies' shareholders alleging failure to disclose (1) risks associated with particular drugs or (2) company behavior—such as off-label and deceptive marketing—that could expose shareholders to substantial losses due to future litigation. There are two general ways that companies could reduce their exposure to such litigation; it is not clear that either type of response would be plausible absent potential penalties from other kinds of litigation. First, companies could more fully disclose drugs' risks of which they are aware in more timely fashions, thereby not only reducing their exposure to shareholder suits but also product-liability and other litigation alleging FTW. A financial downside of such disclosure is potential loss of drug sales due

for the promotion under consideration) would imply higher expected costs than incremental profits only if the incremental profits (\$X) of the contemplated promotional activities were less than \$460 million. In light of the fact that the top ten selling drugs in the United States have annual sales of roughly \$2 billion to \$5 billion (*Drugs.com*, undated), it seems plausible that incremental profits over the course of several years from off-label or deceptive promotion of a single drug could exceed several hundred million dollars.

to more concern by prescribers and consumers about potential injuries. Another downside is triggering or strengthening litigation alleging FTW or deceptive marketing if, for example, a disclosure to shareholders of a drug's risks reveals delay in warning prescribers. Second, a drug company could also lower its exposure to shareholder suits alleging failure to disclose company behavior that leaves it vulnerable to other kinds of litigation by refraining from engaging in such behavior. As discussed earlier in this section, however, some such behavior could be very rewarding financially. There is no apparent indication that the potential costs of shareholder suits is high enough—by themselves—to deter behavior that can greatly increase the profits associated with a drug. Exposure to such lawsuits would, of course, fortify incentives tending to deter off-label promotion and deceptive marketing alleged in the other three kinds of litigation considered in this chapter.

In sum, the related litigation discussed in the present chapter does not simply raise the liability exposure of pharmaceutical companies resulting from personal-injury product-liability litigation. This is because much of the litigation discussed in the present chapter exposes drug companies to potentially large costs for different kinds of acts than are typically central issues in personal-injury, product-liability litigation.

What can we say about the economic efficiency implications of likely corporate responses to liability for deceptive marketing activities and off-label promotion? There may be no plausible case for deception to enhance economic efficiency. Off-label promotion appears more difficult to condemn on efficiency grounds, however, despite the fact that it is illegal. This is because there appear to be both potentially large social benefits and potentially large social costs of the FDA's rules restricting off-label promotion. On the benefit side are potential improvements in clinical information available to prescribers that are discussed in Chapter Three. On the cost side, physician use of drugs for indications not approved by the FDA is widely believed to benefit many patients, and promotion of drugs for off-label use may often improve patient care, particularly to the extent that such promotion involves accurate rather than deceptive information.

In Conclusion

Since 1990, pharmaceutical companies have paid out billions of dollars to defend, settle, and pay judgments in product-liability and related litigation. Looking to the future, it appears that they will remain exposed to similarly large liability costs. The future liability exposures of these companies involve legal actions brought by or on behalf of diverse parties, such as individuals suffering personal injuries, the DOJ, state AGs, consumers, TPPs, and pharmaceutical company shareholders.

An indisputable economic downside of all forms of litigation is the associated transactions costs. Regrettably large transaction costs may be required to achieve such social goals as deterrence of socially undesirable corporate behavior and fairly compensating people for drug injuries, but they undeniably represent very considerable social costs.

We have seen that the stakes involved in actions brought by all of these categories of plaintiffs—with the possible exception of shareholder actions—are likely to be large enough to attract the attention of company decisionmakers when they make decisions affecting drug safety and effectiveness. We should expect, then, that company decisionmakers will respond to their liability exposures—as they perceive them—by seeking and implementing ways to lower their expected liability costs that have acceptable implications for operating profits. And when they make different decisions than they would if they were not exposed to liability, then liability affects economic outcomes. Some likely liability effects seem to enhance economic efficiency and others seem to undermine it. A challenge for public policymakers is to reshape the liability environment to the extent possible so that company responses enhance economic efficiency.

This concluding chapter considers several broad questions by drawing upon and synthesizing facts, inferences, concepts, and ideas presented earlier in this monograph. The next section considers in broad terms how the liability environment for drug companies has changed since about 1990. The sections after that provide an overview of what appears to be the most promising approach to understanding and ameliorating major liability-based sources of inefficient behavior by pharmaceutical companies, followed by examples of liability-based incentives encouraging inefficient behavior by drug companies. I then comment on liability-based incentives that may lead to inefficient behavior by plaintiffs' lawyers and consumers. That discussion is followed by a brief description of preemption law as it applies to different categories of medical products, namely, branded drugs, generic drugs, vaccines covered by the VICP and high-risk medical devices. The penultimate section discusses five major unknowns about the liability environment, many of which appear to be amenable to future research. I conclude with brief summary remarks.

Major Legal Developments Since 1990

Some developments in legal doctrine and practice during the past two decades or so have tended to reduce liability exposure and risks facing pharmaceutical companies and others have tended to increase it.

Product Liability for Personal Injury

Two major developments driven by decisions of the U.S. Supreme Court have reshaped the product-liability exposure of drug manufacturers. First, the court's 1993 decision in *Daubert v. Merrell Dow Pharmaceuticals* seems to have resulted in more extensive judicial efforts to identify and exclude expert testimony on injury causation that judges determine to be unreliable. It is not clear how extensively this more active gatekeeping has affected PPL litigation or whether the effect has tended to improve the reliability of evidence admitted. Second, defendant manufacturers are exposed to lesser amounts of punitive damages in individual trials due to the U.S. Supreme Court decisions in *BMW v. Gore* (1996), *State Farm v. Campbell* (2003), and *Philip Morris USA v. Williams* (2007). As discussed at the end of Chapter Four, however, product-liability exposure and risks facing drug companies continue to be very considerable despite apparent lessening of their exposure to punitive damages.

Other Litigation Pertaining to Drug Safety and Effectiveness

With the possible exception of the shareholder lawsuits, the forms of related liability discussed in Chapter Six appear to have become much more threatening to drug companies since 1990. More specifically, it appears that this period has witnessed major increases in safety-related complaints brought by the DOJ (including criminal complaints against company executives), the AGs of many states, and private plaintiffs. Complaints by state AGs and private plaintiffs often involve state CPAs, the use of which appears to have become much more common since the early 1990s. As discussed in concluding Chapter Six, these three kinds of litigation—and particularly the first two—seem to have substantially increased incentives for drug companies to refrain from off-label promotion and deceptive marketing. It seems plausible, nonetheless, that off-label promotion is in some instances sufficiently profitable that even potential penalties of \$1 billion or more would not suffice to deter almost all off-label promotion and deceptive marketing.

Approach to Policy Improvement

As proposed and discussed in Chapter Two, the best hope for identifying public policy changes that are likely to improve economic efficiency requires major doses of inference. More specifically, policy analysts and policymakers seem well-advised to (1) consider the incentives that are created or strengthened by liability exposure and what company decisions are most likely to be affected by these incentives, (2) identify sources of incentives that encourage socially undesirable company decisions or discourage socially desirable ones, and (3) use public policies to preserve or strengthen incentives that discourage socially undesirable behavior and/or eliminate or attenuate incentives that discourage socially desirable behavior.

Some features of the liability system seem counterproductive with regard to the social goal of improving economic efficiency. Consider first some apparently major, and perhaps the most important, liability-based sources of inefficient manufacturer behavior.

Liability-Based Incentives Encouraging Inefficient Manufacturer Behavior

Incentives to Overwarn

Product-liability doctrine holds firms liable for *failure* to warn, as contrasted with, for example, failure to provide warnings that best promote public health through prescribing decisions and consumer compliance with their doctors' prescriptions. This legal doctrine encourages companies to warn about potential side effects even if they are extremely rare or lacking any reliable scientific support. As reported in Chapter Five, it is controversial within the medical community whether overwarning is a substantial concern from a public health standpoint. The FDA's 2006 *Physician Labeling Rule* (U.S. Department of Health and Human Services, 2006) which asserted preemption of FTW product-liability claims was aimed at mitigating overwarning and its potential social costs, but the limited evidence to date suggests that little, if any, progress has been made (Duke, Friedlin, and Ryan, 2011).

Punitive Damages

Another source of inefficient manufacturer behavior is the perception that companies can be subjected to punitive damages for behavior that promotes economic efficiency. Perhaps the clearest example of efficiency promoting company behavior discouraged by punitive damages is performing *societal-level* cost-benefit or risk-utility analyses to help them decide how best to respond to their liability exposure (Viscusi, 2000; Garber, 2000).¹ More broadly, the fact that companies can be assessed punitive damages for the same behavior in multiple lawsuits increases considerably the stakes for manufacturers and thus tends to increase both socially desirable and socially undesirable economic effects (Garber, 1998, pp. 285–286). Moreover, for many contemplated actions, the likelihood of punitive damages being imposed is extremely difficult for company decisionmakers to assess. A major factor underlying this difficulty is that under the law of many states the circumstances under which punitive damages are available are described with vague terms such as “outrageous,” “oppressive,” and “malicious” (see Chapter Three).

Liability-Based Incentives Encouraging Efficient Manufacturer Behavior

Compliance with FDA Regulations

In most states, compliance with FDA regulations does not provide a shield against product-liability claims, while evidence of failure to comply can be extremely costly to defendants. (See the discussion of RCDs in Chapter Three.) As reported in Chapter Five, there have been several

¹ In the interest of promoting economic efficiency, we want companies to weigh the social costs and social benefits of their responses to liability exposure. In a societal-level cost-benefit analysis, for example, product-related injuries must be valued at their social costs, rather than, for example, the *private* costs to manufacturers of defending lawsuits and compensating injuries through the tort system.

instances in which product-liability litigation has uncovered evidence of companies failing to report adverse events to the FDA (Kesselheim and Avorn, 2007). Imposing liability costs for such behavior tends to discourage it. With the possible exception of restriction of off-label promotion, major FDA regulations pertaining to the period after a drug is approved for marketing in the United States—requiring, for example, post-market clinical studies and complete, honest reporting to the FDA—seem likely to promote efficiency. As discussed at the end of Chapter Six, however, it is possible that, on balance, restrictions on off-label promotion undermine economic efficiency; more specifically, this seems to depend on the balance between honesty and deception in the promotional messages.

Honest and Complete Public Reporting of Risk Information

Kesselheim and Avorn (2007) also present examples of product-liability litigation in which evidence was uncovered of company failures to provide safety-related information to the public (see Chapter Five). Examples include withholding or distorting information about the frequency and severity of side effects and withholding the results of selected clinical trials. Such behavior appears to be inefficient, and discovering such information in the course of litigation and penalizing it through legal liability tend to discourage it. Product-liability actions discovering and penalizing such behavior—and related litigation targeting such behavior—also tend to discourage it.

Liability-Based Incentives Encouraging Inefficient Behavior by Plaintiffs' Lawyers and Consumers

The analyses in this monograph have largely focused on liability-based incentives for decision-makers at drug companies and how their responses are likely to affect economic outcomes and economic efficiency. There are hints of liability-based incentives facing other actors—in particular, plaintiffs' lawyers and consumers—that may also undermine economic efficiency.

Competition Among Plaintiffs' Attorneys to Lead Mass Tort Attempts

Recall from Chapter Four that it is not uncommon for mass tort attempts by plaintiffs' attorneys to result in little compensation for injured people. While lack of compensation does not directly affect economic efficiency, all mass tort attempts involve substantial transactions costs, which are directly relevant to efficiency, borne on both the plaintiffs' and defendants' sides as well as by the public through the court system. As discussed in concluding Chapter Four, it appears that in at least some instances, mass tort attempts fail because at the time that an attempt is launched, there is insufficient evidence for plaintiffs to prevail on injury causation or failure to warn adequately of risks about which the defendants knew or should have known.

Litigation and Consumer Compliance with Prescribed Therapies

Two surveys during the mid-2000s suggest that pharmaceutical litigation may result in many consumers failing to comply with (or “adhere” to) their physicians' prescriptions. First, in 2003, 25 percent of 301 surveyed patients with one or more of eight chronic conditions responded that they would “stop taking the drug immediately” if they “saw an advertisement for litigation over a drug they were taking,” with another 31 percent indicating that they were not sure

(Harris Interactive, 2003, p. 42).² Second, a 2007 survey of 401 psychiatrists reportedly found that (1) 97 percent of them had patients who had stopped taking or reduced their dosages of antipsychotic medications, (2) 52 percent “believed patients took this action due to law firm advertisements about antipsychotic drugs,” and (3) 94 percent of psychiatrists with patients who changed their adherence to their prescribed therapy “reported patient relapse as a result of discontinuing medication” (*Medical News Today*, 2007).

Product-Liability Preemption for Medical Products

As of December 2012, product-liability preemption law—which could be changed by Congress—differed greatly across different categories of pharmaceuticals and high-risk medical devices. More specifically, (1) for branded pharmaceuticals, claims based on none of the three kinds of product defects reviewed in Chapter Three were preempted (*Wyeth v. Levine* made this explicit for FTW claims, which are at the heart of most PPL claims), (2) FTW claims were preempted for generic drugs (*Pliva, Inc., et al. v. Mensing*), (3) for vaccines covered by the National Vaccine Injury Program—see Chapter Four—design defects claims were preempted (*Bruesewitz v. Wyeth*) as were FTW claims if the warnings complied with FDA regulations, and punitive damages were unavailable “absent failure to comply with regulatory requirements, ‘fraud,’ ‘intentional and wrongful withholding of information,’ or other ‘criminal or illegal activity’” (*Bruesewitz v. Wyeth*, p. 5), and (4) for the most strictly regulated medical devices—specifically, devices that have been approved by the FDA through the premarket approval process—legal claims pertaining to safety and effectiveness appear to be broadly preempted (U.S. Supreme Court decision in *Riegel v. Medtronic*, 2008).³

It is far from clear that these differences in preemption law can be rationalized in terms of promoting economic efficiency.⁴ This is hardly surprising because preemption law is driven by congressional intent, and concerns of Congress are not focused on promoting economic efficiency.

Issues to Study and Developments to Monitor

There are several major unknowns about many of the kinds of litigation reviewed in this monograph and their economic effects. Additional research could help in refining the analyses or refuting inferences offered in this monograph and in suggesting conclusions about additional issues. Moreover, future developments in some areas could have major implications for

² In addition, 21 percent of the interviewed patients reported having seen a litigation-related advertisement for a drug they were, in fact, taking (Harris Interactive, 2003, p. 40).

³ The precise extent of preemption embodied in the *Riegel* decision is somewhat unclear. In particular, claims that do not interfere with FDA regulations (or are “parallel” to federal requirements) are not preempted, and since the *Riegel* decision, courts have been sorting out what kinds of claims are and are not preempted (Goss, 2010).

⁴ Some of the legal variation, however, may be rationalized in terms of economic efficiency. Perhaps most clearly, restrictions on common law actions for at least some vaccines appear to promote efficiency relative to the alternative of lack of availability of vaccines; it seems uncontroversial that most, and perhaps all, vaccines approved for sale in the United States easily pass social cost-benefit tests.

economic efficiency. Consider the following five examples that seem to be of substantial social importance.

First, regarding the kinds of litigation considered in Chapter Six, in this study I have not shed any light on the relative prevalence of allegations of different broad kinds, nor have I considered allegations in detail. Systematic information about these issues could be invaluable for sharpening our views about company incentives stemming from this litigation and how companies are likely to alter their behavior in response to those incentives.

Second, there appear to be no empirical studies of judicial gatekeeping focused on pharmaceuticals. Such studies could be very helpful in understanding effects of gatekeeping on corporate decisions. Moreover, they could be helpful (in the pharmaceutical context) for informing the ongoing debate about the wisdom of the U.S. Supreme Court decision in *Daubert v. Merrell Dow Pharmaceuticals* and how the decision has been applied by judges. It appears that neither defendants' nor plaintiffs' advocates are nearly satisfied with the status quo, with defendants believing that they are still inadequately shielded from unreliable evidence and plaintiffs believing that reliable evidence is excluded too frequently.

Third, history and the current state of play regarding medical monitoring for drug-related injuries have apparently not been systematically studied. For example, how influential have the Bechtel criteria (see Chapter Three) been? Are the medical monitoring programs that have been instituted likely to promote or undermine efficiency? How is state law evolving in this area and what are the implications for economic efficiency?

Fourth, there appears to be little, if any, empirical evidence about the extent to which litigation undermines consumer compliance with their prescribed therapies. Pieces of this puzzle might be studied empirically. For example, how often do plaintiffs' lawyers advertising for clients in mass tort attempts make claims about product risks that are not reasonably well supported by medical evidence? If such claims are not uncommon, to what extent do they deter consumers from complying with their doctors' recommendations?

Fifth, under what circumstances would providing compensation for drug-related injuries through no-fault, administrative programs—as with the VICP—be more and less likely to promote efficiency? It seems clear that the high transactions costs of disputing could be greatly lessened through use of administrative compensation for drug-related injuries. Whether such programs would be preferable to the status quo on economic efficiency grounds seems to turn on whether the effects of product liability on manufacturer behavior that would be forgone are sufficiently socially beneficial on balance to outweigh the reductions in transactions costs. As discussed in detail in Chapter Five—and remains true despite the analyses in this monograph—existing information bearing on that question for pharmaceuticals generally is quite incomplete. If administrative compensation is considered for a particular category of drugs, however, the relevant question about deterrence effects would pertain only to drugs in that category. These narrower effects may be more amenable to empirical analysis than effects for all types of pharmaceuticals jointly.

Final Remarks

The economic effects of PPL have been controversial for several decades and will remain so for the foreseeable future. Since 1990, other forms of legal liability have greatly expanded the exposure of pharmaceutical companies to large costs and financial risks, especially regarding

how they promote and market their products. These developments have created new controversies about, for example, economic effects of DOJ actions and use of CPAs by state AGs and private plaintiffs. There are no silver bullets that could eliminate or greatly mitigate socially undesirable economic effects of liability while maintaining or strengthening the socially desirable ones. Nonetheless, in view of the apparently high social stakes, identifying and implementing policy changes designed to improve the liability-based incentives facing pharmaceutical companies could be well worth the considerable efforts required. This monograph offers information that could aid such efforts.

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