INNOVATIVE DRUGS, PRODUCTS LIABILITY, REGULATORY COMPLIANCE, AND PATIENT CHOICE†

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I. INTRODUCTION

Preserving prescription drug innovation is an important policy concern. Innovative drugs can both save lives and contribute to better, healthier lives. At the same time, however, innovation may not always be beneficial and some drugs may pose adverse effects that outweigh their advantages. As a result, it is important to provide safeguards to ensure that drugs are reasonably safe. Additionally, the risks stemming from drugs must be found acceptable by patients.

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Presently, tort litigation and regulation by the Food and Drug Administration (FDA) provide these checks. Concerns have been raised, however, that the tort process, because of its uncertain standards, produces the unintended consequence of discouraging worthwhile innovation. Prescription drug manufacturers maintain that liability risks may cut into their innovative efforts.

Some have suggested that the regulatory compliance defense is a means of reconciling the tension existing among the goals of innovation, regulation, and product liability. This Article examines the regulatory compliance defense and the advantages and objections that have been identified with respect to the defense. In addition, the Article raises a new concern: the impact that a regulatory compliance defense would have on patient choice. Compliance with labeling that meets regulatory standards, even if the labeling information is reasonable to appraise experts about recognized risks, may not be sufficient to provide the information that reasonable patients and their physicians should know about drug risks.

The provision of adequate information about drug risks is especially important and difficult for innovative drugs. Some risks from drugs can be discovered only after the drugs are widely marketed. These risks, discovered during use, may emerge over time and may be the subject of debate and evaluation by experts while patients continue to use the drug.

This Article explores the question of what information should be available to both patients and their physicians with regard to risks stemming from innovative drugs, and the format for providing the information. Specifically, present drug labeling could be supplemented with a digest of current literature on scientific studies that indicate adverse risks, even if experts may differ on how clearly the risk has been demonstrated. The supplementary digest would give physicians, on a regularized basis, access to scientific drug studies about emerging risks associated with pharmaceutical drugs.

In addition to a digest-based informational format, the present system of circulating information can be improved by changing the practice of providing information about drug risks only to physicians, who are then responsible for passing the information on to patients. Instead, drug labeling information should be provided directly to the patient as well as to the physician. This patient labeling information should indicate the principal risks presented, and can provide access to information about new studies in a supple-

mental digest. This system of information sharing would be particularly appropriate and is especially needed for innovative drugs. The initial sale of drugs has been described as Phase IV drug testing, and disclosures to ensure patient consent are especially important in this testing phase.

The supplementary digest and its availability to patients would promote patient choice. In addition, the disclosures should be relevant for determining whether the drug bears adequate warnings to meet liability standards.

II. REGULATORY COMPLIANCE AND ITS MERITS

In evaluating a regulatory compliance defense, it is important to recognize the defense's merits. Generally, the defense's virtues include the potential for encouraging innovation, the provision of clearer standards of conduct for the drug industry, and finally, the avoidance of "information overload."

First, with respect to innovation, medical experts have expressed concern that uncertain liability standards, coupled with litigation costs, may discourage useful drug innovation.[1] In particular, the National Academy of Sciences has found that tort liability may have discouraged the development of new contraceptives and reduced the number of vaccine providers.[2] Other studies have also explained the negative effects of litigation on drug innovation.[3] Moreover, some have questioned jurors' competence to

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[1] *See* Louis Lasagna, *The Chilling Effect of Product Liability on New Drug Development*, *in* THE LIABILITY MAZE 334, 336-47 (Peter W. Huber & Robert E. Litan eds., 1991); *see also* George L. Priest, *The Current Crisis in Modern Tort Law*, 96 YALE L.J. 1521 (1987).

Uncertain liability standards may have had some effect on court decisions which have refused to expand tort liability for pharmaceutical drug companies due to the courts' fear of the potential impact that liability would produce on drug innovation and availability. *See* Brown v. Superior Court, 751 P.2d 470 (Cal. 1988); Shackil v. Lederle Lab., 116 N.J. 155, 561 A.2d 511 (1989); *see also* Teresa M. Schwartz, *Product Liability Reform by the Judiciary*, 27 GONZ. L. REV. 303 (1991-92).

[2] COMM. ON CONTRACEPTIVE DEV., DEVELOPING NEW CONTRACEPTIVES: OBSTACLES AND OPPORTUNITIES 4 (Luigi Mastroianni, Jr., et al. eds., 1990); INSTITUTE OF MEDICINE, VACCINE SUPPLY AND INNOVATION 85, 119 (1985).

[3] *See* W. KIP VISCUSI, REFORMING PRODUCTS LIABILITY 128, 149-54 (1991) [hereinafter REFORMING LIABILITY]; W. Kip Viscusi, *Toward a Diminished Role of Torts Liability: Social Insurance, Government Regulation, and Contemporary Risk to Health and Safety*, 6 YALE J. ON REG. 65 (1989) [hereinafter *Diminished Torts Liability*]; W. Kip Viscusi et al., *A Statistical Profile of Pharmaceutical Industry Liability, 1976-1989*, 24 SETON HALL L. REV. 1418 (1994). *Cf.* Judith Swazey, *Prescription Drug Safety and Product Liability*, *in* THE LIABILITY MAZE 291, 327-28 (Peter W. Huber & Robert E. Litan eds., 1991) (reporting that there is only "sketchy and insubstantial information" available about product liability law's effect on drug safety and concluding that liability has "only a marginal effect on the development of safer drugs").

make risk-benefit determinations for drugs.[4]

The Reporters' Study for the American Law Institute (Reporters' Study) determined that subjecting products to both regulation and tort litigation imposes "special burdens on new products and processes and threatens innovation." The Reporters' Study recommended that regulatory compliance should serve as a presumptive or conclusive defense that would limit tort liability or punitive damages in some circumstances.[5] The FDA seems to meet the criteria identified in the Reporters' Study for agency programs for which a regulatory compliance defense would be appropriate: the FDA is a specialized agency concerned with assessing risks; the agency has "addressed the specific risk[s] at issue in the case[s] at hand"; and the FDA has made "explicit judgment[s] about what type of legal

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[4] *See* Note, *A Question of Competence: The Judicial Role in the Regulation of Pharmaceuticals*, 103 HARV. L. REV. 773 (1990); *see also* Richard B. Stewart, *Crisis in Tort Law? The Institutional Perspective*, 54 U. CHI. L. REV. 184 (1987) (providing overview of institutional perspective).

[5] *See* II Reporters' Study (American Law Institute), *Enterprise Responsibility for Personal Injury* 83-110 (1991) [hereinafter II Reporters' Study]. The Reporters' Study was a report to the American Law Institute (ALI), and was the subject of debate at an ALI meeting. *See* 68 A.L.I. PROC. 1-56, 404-11 (1991). The draft, "Restatement (Third) of Torts: Products Liability," is now in its preliminary stages.

In the case of pharmaceutical drugs, others have also supported some form of a regulatory compliance defense. *See* REFORMING LIABILITY, *supra* note 3, at 128, 149; *Diminished Torts Liability*, *supra* note 3, at 65; Charles J. Walsh & Marc S. Klein, *The Conflicting Objectives of Federal and State Tort Law Drug Regulation*, 41 FOOD DRUG COSM. L.J. 171 (1986); Note, *supra* note 4, at 785-93; *see also* Alan Schwartz, *The Case Against Strict Liability*, 60 FORDHAM L. REVIEW 819 (1992).

There have also been other views on the regulatory compliance defense, and support for expanding liability in other directions. *See* Stephen P. Croley & Jon D. Hanson, *Rescuing the Revolution: The Revived Case for Enterprise Liability*, 91 MICH. L. REV. 683 (1993); Stephen P. Croley & Jon D. Hanson, *What Liability Crisis? An Alternative Explanation for Recent Events in Products Liability*, 8 YALE J. ON REG. 1 (1991); Gregory C. Jackson, *Pharmaceutical Product Liability May be Hazardous to Your Health: A No-Fault Alternative to Concurrent Regulation*, 42 AM. U. L. REV. 199 (1992); Neil K. Komisar, *Injuries and Institutions: Tort Reform, Tort Theory, and Beyond*, 65 N.Y.U. L. REV. 23, 76 (1990); Howard A. Latin, *Problem-Solving Behavior and Theories of Tort Liability*, 73 CAL. L. REV. 677 (1985); Robert A. Prentice & Mark E. Roszkowski, *"Tort Reform" and the Liability "Revolution": Defending Strict Liability in Tort for Defective Products*, 27 GONZ. L. REV. 251 (1991-92); *see also* Schwartz, *supra* note 1, at 308-10 (lack of data to show effects and extent of liability impact).

For an earlier discussion of strict liability for prescription drugs, see Richard A. Merrill, *Compensation for Prescription Drug Injuries*, 59 VA. L. REV. 1 (1973).

For a general criticism of direct regulation's ability to promote safety, see Richard J. Pierce, Jr., *Encouraging Safety: The Limits of Tort Law and Government Regulation*, 33 VAND. L. REV. 1281, 1308-19 (1980) ("It is hard to conjure up a system of accident cost control more irrational and less reflective of social values than the present tort system. Congress, however, has proven itself equal to the task through the values and allocative effects implied in OSHA's organic act.").

controls are appropriate" for prescription drug manufacturers.[6] This conclusion is buttressed by the fact that companies must "publicly disclose" to the agency material information concerning risks involved with regulated products.[7]

The regulatory compliance defense also gathers force from the apparent unfairness of holding drug manufacturers liable for failures to provide warnings, even though the FDA did not require warnings, and despite the fact that the agency may even have discouraged the company from providing a warning. Some reported cases reflect FDA efforts to discourage warnings.[8] These examples of a company being caught in the middle appear inconsistent with a tort system generally based on fault.[9]

Moreover, courts may be under a misapprehension about the extent of the FDA's permissiveness in allowing manufacturers to add warning information to the labeling. Courts continue to view the FDA labeling as minimal,[10] and view FDA regulations as permitting manufacturers to strengthen warnings without prior FDA approval.[11] While the relevant FDA regulation is not without ambiguity, in practice the agency has not viewed the drug label as a minimal statement of the risks.[12]

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6 *See* II Reporters' Study, *supra* note 5, at 95-97, 110.

7 *Id.* at 97.

8 *See* Feldman v. Lederle Lab., 97 N.J. 429, 479 A.2d 374 (1984) (*Feldman I*); Wooderson v. Ortho Pharmaceutical Corp., 681 P.2d 1038 (Kan.), *cert. denied*, 469 U.S. 965-66 (1984); Brochu v. Ortho Pharmaceutical Corp., 642 F.2d 652 (1st Cir. 1981); Salmon v. Parke, Davis & Co., 520 F.2d 1359 (4th Cir. 1975); McEwen v. Ortho Pharmaceutical Corp., 528 P.2d. 522 (Or. 1974).

9 *See* Thomas Scarlett, *The Relationship Among Adverse Reaction Reporting, Drug Labeling, Product Liability and Federal Preemption*, 46 FOOD DRUG COSM. L.J. 31 (1991) (noting that these cases are not very common, and that companies do not usually face much resistance from the FDA).

10 *See* Feldman v. Lederle Lab., 125 N.J. 117, 592 A.2d 1176 (1991), *cert. denied*, 112 S. Ct. 3027 (1992) (*Feldman II*); Wooderson v. Ortho Pharmaceutical Corp., 681 P.2d 1038 (Kan.), *cert. denied*, 469 U.S. 965-66 (1984). In New Jersey, compliance with FDA regulations is presumptive of non-liability. N.J. STAT. ANN. § 2A:58-C4 (West 1987).

11 See *supra* note 8 for a list of cases. In *Feldman II*, the New Jersey Supreme Court reaffirmed the position adopted in *Feldman I*, that the FDA labeling establishes minimal requirements and that 21 C.F.R. § 201.57(e) (1990) allows manufacturers to strengthen risk warnings in labeling before FDA approval of the labeling change. *Feldman II*, 125 N.J. at 146-53, 592 A.2d at 1193-95. *See* 21 C.F.R. § 201.57(e) (1993) (providing current codification of the 1990 regulation construed by the *Feldman II* court); *see also id.* § 314.70(c)(2)(i) (requiring approved-drug applicants to submit supplemental information when the applicant, *inter alia*, strengthens or adds to labeling warnings). Later, in *Feldman III*, the court pointed out that drug manufacturers' liability would turn on the jury's determination of whether a reasonable manufacturer would have provided warnings in addition to those required by the FDA. Feldman v. Lederle Lab., 132 N.J. 339, 347-48, 625 A.2d 1066, 1070 (1993) (*Feldman III*).

12 *See* Richard M. Cooper, *Drug Labeling, and Products Liability: The Role of the Food*

Instead, the agency has sought to control the information that drug manufacturers must provide with their products. The agency has been urged, however, to clarify its position on the extent to

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and Drug Administration, 41 FOOD DRUG COSM. L.J. 233, 235-38 (1986); Scarlett, *supra* note 9, at 32, 40 (stating that the FDA views labeling "as the principal means by which the agency communicates the conditions of use . . . found by it to be safe and effective," and regards the labeling "as fully adequate for the purpose of informing physicians of all necessary information," although the agency would concede "labeling might lag behind developments.").

A number of cases illustrate the difficulties in applying the FDA regulation. In *Feldman I*, the manufacturer sought approval from the FDA to warn of a risk of tooth discoloration stemming from use of the manufacturer's form of tetracycline, but the FDA, through its medical officer, advised by phone and letter against the warning because the matter was under study and because of the absence of clinical evidence. 97 N.J. at 439, 479 A.2d at 379. When the warning was later added to tetracycline drugs generally, the FDA discouraged the company from adding the warning for the particular drug, and approved the inclusion of the warning some months later, only after reports were received of discoloration. *Id.* at 439-40, 479 A.2d at 379.

In *Wooderson v. Ortho Pharmaceutical Corp.*, the manufacturer pointed out that the FDA had earlier declined to permit label changes in spite of another manufacturer's letter proposing changes that touched on the possibility of contraceptive-linked kidney problems. 681 P.2d 1038, 1057 (Kan.), *cert. denied*, 469 U.S. 965-66 (1984). Accordingly, Ortho argued that the FDA had determined that warnings are not needed for contraceptive-linked kidney disease health risks. *Id.* As such, Ortho argued that it should not be held liable for its failure to warn of potential kidney problems stemming from the use of Ortho's oral contraceptive. *Id.* The Kansas Supreme Court, however, explained that the FDA cannot be held to have made a dispositive ruling in responding to requests for labeling changes. *Id.*

In *Brochu v. Ortho Pharmaceutical Corp.*, the labeling failed to refer to a recent study in the *British Medical Journal* not available to an FDA drafting group that indicated a possibly greater risk from the drug at issue. 642 F.2d 652, 658-59 (1st Cir. 1981). In rejecting the argument that the study had methodological problems, the court noted that other studies referred to in the labeling appeared to have less than medical certainty and the manufacturer had been "choosy in the wrong direction" in applying the standard. *Id.* at 659 n.14.

In *McEwen v. Ortho Pharmaceutical Corp.*, the labeling failed to disclose a report in the *British Medical Journal* on clotting disease from oral contraceptives. 528 P.2d 522, 531 (Or. 1974). In addition, the label failed to disclose another report focusing on animal study results. *Id.*

In *Wells v. Ortho Pharmaceutical Corp.*, the trial court, sitting without a jury, found warnings inadequate because of the manufacturer's failure to refer to the possibility of the product's association with birth defects, as had been indicated in published articles and an NIH study. 615 F. Supp. 262, 271-72 (N.D. Ga. 1985), *aff'd*, 788 F.2d 741 (11th Cir.), *cert. denied*, 479 U.S. 950 (1986). The district court reached this decision notwithstanding the FDA advisory committee decisions that the product's association with health risks was not so established as to warrant a warning. *Id.* at 279-81. Moreover, the court rejected the argument that warnings would discourage use of a beneficial product because the appropriateness of a product "should be determined by users . . . and their physicians with access to all relevant information, not by manufacturers." *Id.* at 295. The Eleventh Circuit affirmed, noting a difference between evidence that is legally sufficient and evidence that is conclusive for the purpose of resolving issues to a medical certainty. Wells v. Ortho Pharmaceutical Corp., 788 F.2d 741, 745 (11th Cir.), *cert. denied*, 479 U.S. 950 (1986).

which it seeks to exercise total control over the content of the drug labeling.[13] For example, FDA regulations allow a manufacturer to make a change in the labeling at the same time the manufacturer requests FDA approval,[14] but the FDA expects this procedure to be used only in unusual cases, and even then approval of the change by the FDA is still required. Understandably, drug manufacturers are influenced by the agency's views.

Finally, the regulatory compliance defense can be viewed as beneficial in its prevention of information overload. The FDA seeks to provide labeling that adequately provides physicians with information needed for safe and effective care.[15] This does not mean that drug companies must provide information about all drug-associated risks. Rather, the FDA regulations call for labeling changes to include a warning as soon as there is "reasonable evidence of an association of a serious hazard with a drug," although a "causal relationship" need not be proved.[16]

Under FDA rules, labeling is to provide advice on "known hazards and not theoretical possibilities."[17] While the FDA standard for determining when labeling changes are needed is not always clear,[18] the FDA does not believe that more labeling is

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13 *See* Cooper, *supra* note 12, at 238-39. The FDA might reconsider regulations to preclude labeling changes without FDA approval, and allow unilateral action by companies to warn of risks only in circumstances identified by the FDA. *Id.* For instance, in such emergencies, warnings could be provided by better means of communication, such as press releases. *Id.*

14 21 C.F.R. § 201.57(e) (1993) ("The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug."); *Id.* § 314.70(c)(2)(i) (requiring manufacturer to supplement information about an approved drug whenever the manufacturer strengthens, or adds to label warnings).

15 21 C.F.R. § 201.56 (1993). *See Wells*, 615 F. Supp. at 295 (appropriateness of drug use "should be determined by the users . . . and their physicians with access to all relevant information, not by manufacturers").

16 *Id.* § 201.57(c). *See Feldman II*, 125 N.J. at 158, 592 A.2d at 1197 (Garibaldi, J., dissenting) (favoring a regulatory compliance defense and characterizing the FDA's role as including a process wherein optimal assessments are made with regard to new drugs and drug safety).

17 *Id.* § 201.57(d). In *Feldman v. Lederle Laboratories*, for example, the FDA sought clinical evidence of adverse effects of a specific drug before allowing a warning, even though adverse effects had been found in similar drugs. *Feldman I*, 97 N.J. at 439, 479 A.2d at 379.

18 *See* Jeffrey N. Gibbs & Bruce F. Mackler, *Food and Drug Administration Regulation and Products Liability: Strong Sword, Weak Shield*, TORT & INS. L.J. 194, 232 (1987) ("FDA regulations, for the most part, do not specify the circumstances which compel a manufacturer to modify its labeling to reflect [post-approval] increased knowledge.") (footnote omitted); *see also* Ellen J. Flannery, *Reporting Foreign ADRs and ADRs in Phase IV Studies, and the Significance of Causality Assessment*, 46 FOOD DRUG COSM. L.J.

necessarily better.[19]

The agency seeks to prevent overload of the label with so much information that it distracts attention from what is important. Moreover, the FDA seeks to permit comparisons among drugs by physicians. Information about remote and poorly substantiated risks may result in a drug appearing more dangerous than another drug, even though the drug is not as hazardous as made to appear. Thus, to prevent overload and permit comparisons, FDA labeling tends to set "precise" controls with minimal freedom for the manufacturers to make additions.[20] This FDA policy would seem to support making compliance presumptive, possibly dispositive, and arguably even preemptive.[21] The courts, though, continue to reject regulatory compliance as a dispositive defense.[22]

III. Concerns About a Regulatory Compliance Defense

There are concerns that weigh against a ready recognition of a regulatory compliance defense. As the ALI Reporters' Study recognized, the regulatory compliance defense should apply only if the agency has adequate means of obtaining information and the regulated company supplies the requisite material to the agency. With regard to the FDA, drug companies must submit material relevant to the product's risks, and the companies face penalties if they fail to do so.[23]

Nonetheless, there can be concerns about the adequacy of the agency's resources to evaluate fully the information that the manufacturers provide with their products. This concern increases if the

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43, 50-55 (1991) (highlighting ambiguities in FDA standards for reporting foreign adverse drug effects).

19 *See* Cooper, *supra* note 12, at 237.

20 *See id.* at 236.

21 *See* Walsh & Klein, *supra* note 5.

22 Courts have not regarded FDA drug labeling as preemptive, noting the absence of any express federal intention to preempt, and the states' compensatory interest. *See* Feldman v. Lederle Lab., 97 N.J. 429, 479 A.2d 374 (1984) (*Feldman I*); Feldman v. Lederle Lab., 125 N.J. 117, 592 A.2d 1176 (1991) (*Feldman II*), *cert. denied*, 112 S. Ct. 3027 (1992); *cf.* Ferebee v. Chevron Chem. Co., 736 F.2d 1529 (D.C. Cir.), *cert. denied*, 469 U.S. 1062 (1984). The patient access goal of labeling as a means of ensuring informed consent identifies a distinct additional goal for tort labeling that goes beyond the expert evaluation aim that seems to underlie the FDA's labeling goals. As suggested below, the tort goal can be promoted by having separate supplementary labeling of risks in a way that guards against the risk of overload, the federal concern. The existence of distinct goals and a means to reconcile them further weakens the basis for preemption.

23 *See* Gibbs & Mackler, *supra* note 18, at 213-14, 216-17, 231-35, 237-42.

agency is to be placed in the position of being the only source of review to evaluate the need for disclosures.[24] Moreover, objections to the regulatory compliance defense have been raised on the grounds that agencies can be "captured" by the industries that they regulate and rely upon for information.[25]

The case for a regulatory compliance defense is strongest when the agency decision is a reasoned one for which the agency is publicly accountable. The very process of having to explain the decision and anticipate objections promotes a reliable decision. Accordingly, more weight is appropriate for agency decisions, such as rulemaking, which are public, reasoned, and judicially reviewable.

The initial FDA approval of a new drug receives considerable attention from both within the agency and from advisory committees, and is accompanied by a public summary of the risks and benefits of the drug.[26] While these approvals are not often subject to judicial challenge,[27] the expert attention and visibility of the decisions rightly warrant considerable deference.[28] In practice, the FDA's initial approval of a drug actually receives considerable deference from the courts in tort litigation.[29]

The "great majority" of drug liability cases concern not the ini-

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[24] *See* Cooper, *supra* note 12, at 240 (noting that the agency needs to decide whether it wishes to devote the resources involved in a role of exclusively determining labeling disclosures).

[25] *See* II Reporters' Study, *supra* note 5, at 100. The Reporters' Study viewed disclosure of risk information as a means to alleviate this concern. *See id.*; *see also infra* note 73 (discussing disclosure standards).

[26] *See* Gibbs & Mackler, *supra* note 18, at 222-25. The FDA action is licensing, and no public announcement of the basis for the agency decision is legally required.

[27] *See* PETER B. HUTT & RICHARD A. MERRILL, FOOD & DRUG LAW 532 (2d ed. 1991) (reporting that only one FDA decision approving a drug had been challenged in court but the challenge was unsuccessful).

[28] Gibbs & Mackler, *supra* note 18, at 223. Still, even at the time drugs are initially approved, there may be a need to supplement the basic labeling with information of any studies or reports that provide a reliable basis for watching for other additional risks. *See* S. REP. NO. 102-215, 102d Cong., 1st Sess. 82 (1991) (quoting letter from Congressman Ted Weiss, which stated that the FDA did not include reports of certain effects when the drug Oroflex was initially approved; the drug was later removed).

[29] Prescription drugs benefit from Restatement (Second) of Torts, § 402 cmt. k, under which unavoidably unsafe products are not considered unsafe if they bear adequate warnings. In *Brown v. Superior Court*, for example, strict liability was precluded for prescription drugs. 751 P.2d 470, 477 (Cal. 1988). Some cases, though, support allowing a design defect in some limited circumstances. *See* Brochu v. Ortho Pharmaceutical. Corp., 642 F.2d 652, 654-55 (1st Cir. 1981); Rohrbough v. Wyeth Lab., Inc., 719 F. Supp. 470, 476-77 (N.D. W. Va. 1989), *aff'd*, 916 F.2d 970 (4th Cir. 1990); West v. Searle & Co., 806 S.W.2d 608, 612-13 (Ark. 1991); *see also* John P. Reilly, *The Erosion of Comment K*, 14 U. DAYTON L. REV. 255, 258 (1989).

tial approval of the drug by the FDA, but the question of the need to add warnings about risks identified after marketing.[30] An FDA medical officer's decision finding no need to add a warning to the labeling with regard to these post-approval risks is a low visibility decision that does not involve a public explanation. Because the agency decision not to require an additional warning is inaction, the non-decision would ordinarily be a matter committed to agency discretion and not subject to judicial review.[31]

The reported cases illustrate that the FDA's decisions to not include risk information in the label have involved FDA medical officers' communications with drug companies via letters and phone calls.[32] While these letters, and the information submitted to the agency, may ultimately become public information if a request is made, these requests are likely to be made only later, if further problems are attributed to the drug.[33]

Presently, drug manufacturers have an interest in adding warnings to the labeling because the warnings help protect the manufacturer from liability.[34] If FDA labeling precludes the need for additional warnings, drug manufacturers may become reluctant to include the warnings and may even seek to dissuade the medical officers in calling for them.[35]

Finally, patient choice is a concern that weighs heavily against a regulatory compliance defense. The law recognizes that a reasonable physician's determination can differ from that of a reasonable patient, but the law also recognizes that a physician must provide the patient with disclosures sufficient to enable the patient to give informed consent. Many leading medical malpractice cases utilize a reasonable patient standard for determining whether informed

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30 *See* Gibbs & Mackler, *supra* note 18, at 228 (stating that "a review of . . . cases shows that the great majority of suits are predicated on actions or omissions that took place *after* the drug or device entered the market").

31 Heckler v. Chaney, 470 U.S. 821, 835-37 (1985). The FDA action was characterized as a "non-decision," and one that did not preclude the manufacturer from being responsible for providing additional warnings. Feldman v. Lederle Lab., 125 N.J. 117, 196, 592 A.2d 1176, 1196 (1991), *cert. denied*, 112 S. Ct. 3027 (1992) (*Feldman II*).

32 *See* Feldman v. Lederle Lab., 97 N.J. 429, 439, 479 A.2d 375, 379 (1984) (*Feldman I*) (describing defendant's communications with the FDA, including letter writing and phone calls, in response to reports that defendant's product produced adverse health risks).

33 The information should be available under the Freedom of Information Act, 5 U.S.C. § 552 (1988 & Supp. III 1992).

34 See Scarlett, *supra* note 9, at 35-37, on the manner in which the dynamics of product liability suits encourage disclosures.

35 See Salmon v. Parke, Davis & Co., 520 F.2d 1359, 1363 (4th Cir. 1975), for an example of a company resisting an FDA suggestion for a change in the drug labeling.

consent had been obtained.[36] In effect, the law recognizes that the patient has a right to say no to treatment that is customary and generally accepted by experts. The law also assumes that a reasonable patient and a reasonable expert may have different views on acceptable risks.[37]

Accordingly, the need to safeguard patients' rights to express an informed consent supports the refusals of courts to make regulatory compliance a defense. When drug risks appear on the label, the physician has access to the information, and indirectly the patient has access because of the physician's responsibility to the patient. If the drug company does not have to provide the information in drug labeling, the physician will not be able to provide the information to the patient and will be unable to ensure informed consent. Moreover, the physician will not be able to exercise her own best judgment to advise on the significance of the emergent risks.[38]

In recognizing a patient's right to informed consent, the law reflects goals beyond the general goal of promoting social utility.[39] Tort law can promote social utility, but it can also aim to correct harms that offend the sense of fairness and justice.[40] While this goal can overlap with utilitarian factors, its aims rest on a different

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36 Canterbury v. Spence, 464 F.2d 772, 786-88 (D.C. Cir. 1972).

37 The right to informed consent can also be seen as essentially a right to participate in the process of decision making, which may affect the measure of damages. *See* Aaron D. Twerski & Neil B. Cohen, *Informed Decision-Making and the Law of Torts: The Myth of Justiciable Causation*, 1988 U. ILL. L. REV. 607, 607-08.

38 Another reason why the establishment of a regulatory compliance defense could narrow information disclosures stems from the fact that the FDA's ability to take enforcement action against drug companies for failure to make a disclosure may require a higher threshold of proof than that needed to support a tort verdict. *See generally* Gibbs & Mackler, *supra* note 18, at 232-33.

39 *Compare* United States v. Carroll Towing Co., 159 F.2d 169, 173 (2d Cir. 1947) (focusing on the probability and magnitude of harm and the burden of protecting against such harm in determining defendant's standard of care in negligence case) *with* Conway v. O'Brien, 111 F.2d 611, 612 (2d Cir. 1940) (focusing, in negligence case, on "how loudly [the defendant's] conduct cries for censure"). Additionally, compare RICHARD A. POSNER, ECONOMIC ANALYSIS OF THE LAW (1972) with William H. Rodgers, Jr., *Negligence Reconsidered: The Role of Rationality in Tort Theory*, 54 S. CAL. L. REV. 1 (1980).

40 *See* Jules L. Coleman, *Tort Law and the Demands of Corrective Justice*, 67 IND. L.J. 349 (1992); Richard A. Epstein, *Defenses and Subsequent Pleas in a System of Strict Liability*, 3 J. LEGAL STUD. 165 (1974); George P. Fletcher, *Fairness and Utility in Tort Theory*, 85 HARV. L. REV. 537 (1972); George P. Fletcher, *The Search for Synthesis in Tort Theory*, 2 J.L. & PHIL. 63 (1983); Christopher H. Schroeder, *Corrective Justice and Liability for Increasing Risks*, 37 UCLA L. REV. 439 (1990); Ernest J. Weinrib, *Toward a Moral Theory of Negligence Law*, 2 J.L. & PHIL. 37 (1983); Richard W. Wright, Symposium, *Corrective Justice and Formalism, The Care One Owes One's Neighbors, Substantive Corrective Justice*, 77 IOWA L. REV. 625 (1992).

basis.[41] In the case of products such as drugs that are purchased voluntarily by the consumer, the transaction is essentially consensual. The terms of the implicit contract between the consumer-patient and the manufacturer frame the consideration of the fair and just allocation of liability.[42]

Patient choice is especially pertinent in the context of experimental drugs. Before drugs are approved by the FDA, and while they are being clinically tested, the need for patients' informed consent is well-recognized. When innovative drugs are first approved for sale, the drugs still have an experimental quality. The pre-approval testing of drugs on a limited number of subjects cannot fully identify the range of adverse effects that can occur in the general population. For this reason, the initial marketing of a drug has been described as Phase IV of drug testing.

Some of the adverse effects (and benefits) of a drug are discovered only after use on the population at large.[43] Therefore, patients using newly-marketed drugs should have access, at least through their physician, to issues about emerging risks, so that they can make an informed decision about whether to participate in what is, inevitably, an extension of the experimental testing of the drug.[44]

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41 *Compare* I Reporters' Study (American Law Institute), *Enterprise Responsibility for Personal Injury* 24-25 (1991) *and* II Reporters' Study, *supra* note 5, at 79 (corrective justice based on absolute standards is not a primary goal of torts) *with* 68 A.L.I. PROC. 44-45 (1991) (comments of Professor Alan Schwartz) (stating that "while we don't use the words 'corrective justice' a whole lot in the Report, our views about consent and the notion of wrongdoing seem to be consistent with corrective justice notions"). The two goals can overlap with respect to transactions like drug purchases that involve a consensual relationship. In consensual transactions, cost factors and tradeoffs can enter into what consumers want. Furthermore, from a utilitarian perspective, consent itself can be seen as a good that patients value. Nonetheless, these theories are different in the factors that create the duty, i.e., consent or efficiency balancing. Moreover, under a corrective justice approach, a wrong has been done that needs some remedy even if the result is socially beneficial. For example, even if a patient receives beneficial medical care, a wrong has been done if there was no consent to the medical procedure. Mohr v. Williams, 104 N.W. 12, 15-16 (1905).

42 *Mohr*, 104 N.W. at 15. Richard A. Epstein, *Medical Malpractice: The Case for Contract*, 1976 AM. B. FOUND. RES. J. 87, 108-13.

43 50 Fed. Reg. 7471 (1985) (codified at 21 C.F.R. § 314.80 (1993)). See *infra* Part VI for a proposal on furnishing labeling information to patients during Phase IV marketing.

44 Informed consent, ordinarily in writing, is required for experimental drugs tested at the pre-approval stage. 21 U.S.C. § 355(i) (1988 & Supp. IV 1993); 21 C.F.R. Part 312 (1993) (Investigational New Drug Application). Phase IV testing is not experimental testing in one sense because the drugs are thought to be of benefit to the immediate user. On the other hand, the drugs pose unknowable risks, determinable only by experience, and the use of the drugs by the immediate users may reveal risks that can benefit others later.

The adequacy of the scientific support needed to demonstrate a risk can also emerge over time and build on prior information.[45] In some areas, uncertainties may persist about the existence of an effect because it is difficult to develop cost-effective studies to resolve them.[46] In this setting, the process of allowing access to the fact that expert debate and uncertainty exist is preferable to a single determination of when evidence indicates a recognizable risk.

When a drug's additional adverse effects are discovered after the drugs have been marketed, there may be some lag time in disclosures while the risks are evaluated and confirmed by other studies.[47] A similar lag time also exists in the evaluation of drugs before they are approved, while studies are done and reviewed. That lag time for unapproved drugs delays the worthy drugs as well as the problem drugs, but the delay is justified by the need for data necessary to a final determination.

When drugs are already on the market, however, patients continue to use them while uncertainties are being sorted out and evidence accumulated to resolve issues, to the extent that the issues can be resolved. Many adverse reactions to drugs are discovered only after a drug is marketed to the general public.[48] In this situation, there should be some disclosure about the possibility of discovering new effects and about any risks identified in scientific studies that may concern experts, even if the support is not sufficient to be generally accepted or to establish the risk clearly. The patients should have a way to make a choice about how much uncertainty concerns them.[49]

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[45] Skill v. Martinez, 91 F.R.D. 498 (D.N.J. 1981) (jury finding upheld on need for warning about risks of oral contraceptives to women who smoked, even though based on preliminary studies, and even though researchers would have liked a "larger sample"), *aff'd*, 677 F.2d 368 (3d Cir. 1982).

[46] *See* Joseph Sanders, *The Bendectin Litigation: A Case Study in the Life Cycle of Mass Torts*, 43 HASTINGS L.J. 301 (1992) (examining the processes, i.e., epidemiological studies, utilized in testing new drugs).

[47] *See* Scarlett, *supra* note 9, at 40 ("The [Food and Drug] [A]gency would concede that the labeling might lag behind developments.").

[48] *See* GOODMAN AND GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS 64 (Alfred G. Gilman et al. eds., 8th ed. 1990) (explaining that one-half of drugs' adverse effects are reported by physicians after approval). One study reported that 51.5% of drugs approved in a ten-year period had serious post-approval risks. U.S. GENERAL ACCOUNTING OFFICE, FDA DRUG REVIEW POST-APPROVAL RISKS 1976-85, 3 (1990).

Unexpected fatalities can also occur in well-designed clinical trials before drugs are approved. *See* John Schwartz & David Brown, *A Deadly Medical Gamble: Test of Promising Drug Turns Into "Calamity,"* WASH. POST, July 8, 1993, at A1 (unexpected deaths in Phase III clinical tests for fialuridine).

[49] See *infra* Part VI for a discussion of the virtues of supplying labeling information directly to patients. The supplementary disclosures described below would, however,

IV. RECONCILING PATIENT CHOICE WITH FDA GOALS AND INNOVATION

If the analysis suggested here is correct, a regulatory compliance defense is problematic if the manufacturers' FDA-approved labeling disclosures to physicians do not provide all the information reasonable patients want and need to know to make an informed consent to drug use. On the other hand, seeking to ensure patients' informed consent as a drug labeling goal can add to the problems of information overload that already concern the FDA. Moreover, some may question whether reasonable patients really want information on debated risks beyond what the FDA considers necessary, and, indeed, whether the reasonable patient's interest can ever be reliably determined. Some help in addressing these concerns can come from viewing the patient's interest as an access goal, and in considering whether disclosures can be made in a way that guards against overload by ensuring adequate prominence to the information that is required by the existing FDA regulations.

Identifying the information a reasonable patient wants to know can be difficult. Courts have not provided any specific test to identify the disclosures that a reasonable physician must provide to reasonable patients for the purpose of ensuring informed consent. Instead, the jury has been relied upon as an especially suitable source for determining the "uniquely human and necessarily situational ingredients that contribute to a specific doctor-patient exchange of information."[50] Moreover, the need to decipher in advance which risks are of interest to reasonable patients encounters the "Faust" effect—a tendency to discount remote risks, at least until they become a present concern.[51]

Identifying the terms of patients' understanding is, thus, an elusive goal, and it is especially hard to identify the appropriate standard for disclosure of uncertain drug risks. The patient is a non-expert and seeks the provision of medical care and drug therapy by those more expert and knowledgeable than herself. Be-

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be updated only periodically, still leading to some lag time in providing information. *See infra* note 50 and accompanying text (discussing courts' inability to articulate standards for determining whether information must be disclosed to patients). Nonetheless, physicians and their patients would at least know that the information that they obtain will be current as of a specified period.

50 Arato v. Avedon, 858 P.2d 598, 607 (Cal. 1993). The court rejected the need for a jury instruction requiring disclosure of statistical life expectancy data and instead favored an instruction based on the general standard, leaving the nature of the disclosure needed to the judgment of the jury. *Id.*

51 *See* GUIDO CALABRESI, THE COST OF ACCIDENTS 57 (1970); Pierce, *supra* note 5, at 1301.

cause the patient does not have the background to identify and specify the precise information needed for obtaining her own informed consent, hypothetical consent, based on an estimate of what the patient would accept if the patient knew more, becomes important.[52] The access role, identified here, inevitably reflects a personal estimate of what patients would seek in this setting.

One might assume that reasonable patients would be concerned, at some point, about the additional costs of providing the information, and the drawbacks of having so much information about remote risks that the overload obscures what is relevant. On the other hand, an estimate of what reasonable patients want must also reflect the strong contemporary interest of patients, and consumers, in being able to *choose* with respect to matters that affect them and their health.[53] Patients, though, also vary. In the end there may be no single, permanent bright line test for what the reasonable patient wants.

Instead, what the reasonable patient wants to know may be better thought of as involving a range of information from major risks, about which most patients clearly want to know, to matters where patients vary and are uncertain about what they want to know. Disclosures may similarly need to cover a range and reflect a process. Disclosures of the recognized major risks need to be more prominent; information about emerging and debated risks should provide access to the fact of the debate and the scientific process of dealing with uncertainty.

In the end, what patients want to know would seem to have two aspects. Patients want to be informed about the well-established risks so that the patients can have an *opportunity* to say no to incurring the risk even if in the end the patients generally decide to accept the risk. In addition, for a similar reason of having the opportunity to opt-out, patients should have some access to information about debated risks for which some experts find reliable

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52 *See* 68 A.L.I. PROC. 44-45 (1991) (comments of Professor Alan Schwartz) (explaining that "if a person doesn't actually consent, it's a fair move to ask what they would have consented to. So we ask whether the liability standards we recommend would have been consented to by fully informed and rational persons, and we believe that many of them would be"). In the absence of hard information, a personal estimate often enters the estimate of what a reasonable patient seeks, as it has here. Whether the estimates, once stated, are accepted is one test for how well they reflect the real but unarticulated views of patients.

53 *See, e.g.*, Roe v. Wade, 410 U.S. 113 (1973). President Clinton's Health Plan in its present form emphasizes a means for patients to be able to choose their own physician. Courts have also recognized patients' right to choose those who will act as their physicians.

scientific evidence for an association. This holds true even if the risk would not yet be accepted as established by experts or physicians generally, and may never be established.

Access to this additional information, rather than a description of all the information, is the important factor in this context. Given the cost and limited value of this additional information, patients are not likely to want to know as much about these debated risks as they want to know about the recognized risks. But I suspect that, at a minimum, patients want to know that their doctors have opportunities for considering emerging risks debated among experts. Based on that information, physicians can give the patient their best advice on whether the drug is appropriate for the particular patient.[54]

The FDA now seeks to require labeling that will give physicians the information they need without the drawbacks of information overload. While this labeling should continue to be provided prominently in the format the FDA considers appropriate, consideration should be given to allowing a supplementation of the labeling for the purpose of providing a digest of scientific studies reported in the current literature about adverse reactions from the use of the drug. The digest would clearly indicate that it is a catalog of reported risks being monitored or watched by the manufacturer, but that the FDA has not yet made any decision on the extent to which an association had been established, or on any need to change the basic labeling directions and warnings to reflect the reports.

The list would provide information and could facilitate access to scientific studies raising possible risks that physicians might wish to consider, to whatever extent deemed appropriate in treating and advising their patients. Moreover, the manufacturer could include the supplementary list without conceding that the enumer-

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[54] Courts have referred to the role of warnings on drugs as allowing the doctor to make an informed choice about drug use on behalf of the patient. The law also recognizes that it is the patient's decision whether to undertake any medical or drug therapy. Because such decisions must be made on an informed basis, the current state of the law suggests a need for warnings on drugs that enable physicians and patients to make an informed choice about the risks involved with prescription medication. *See* Wells v. Ortho Pharmaceutical Corp., 615 F. Supp. 262, 295 (N.D. Ga. 1985) (appropriateness of drug use "should be determined by the users . . . and their physicians with access to all relevant information, not by manufacturers"), *aff'd*, 788 F.2d 741 (11th Cir.), *cert. denied*, 479 U.S. 950 (1986).

Moreover, as suggested below, patients may also want some direct access to this information, an interest that can be met through providing drug labeling information directly to patients. *See infra* Part VI (proposing a system wherein medication labeling information would be supplied directly to patients).

ated risks are indeed associated with the drug.[55]

Reports would be included when a reasonable expert has identified sufficient evidence to suggest a possible association. That evidence should be based on accepted scientific techniques. Publication in a recognized scientific journal should warrant inclusion in the digest. There may also be other limited occasions when unpublished studies or information, known to the manufacturer, might warrant a digest report if they represent reliable scientific evidence.[56] Case reports concerning adverse reactions would not need to be included in the label, although it would be desirable to have the digest include some tabulation of the reports that would permit noting any significant patterns of adverse reactions.

The digest's format would reflect its role in providing access to sources of information—about reportable recent studies—rather than being an evaluative or exhaustive report. Exactly what the format might be is an open point, and the description here is meant only to be suggestive. The list, for example, might provide only a capsule statement of the author's conclusions in the published studies. It might also be limited to the principal publications that the FDA expects drug manufacturers to monitor. The extent to which other literature needs to be reported has been a debated issue in products liability cases and elsewhere, especially with regard to articles appearing in obscure foreign journals. Perhaps coverage of these other reports should be provided only if the report is sufficient to warrant an alert report regarding unexpected reactions, consistent with the FDA's criteria.[57]

The listings might also be organized alphabetically by type of

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55 *See* 21 C.F.R. § 314.80(*l*) (1993) ("A report or information submitted . . . under this section . . . does not necessarily reflect a conclusion by the applicant or FDA that the report or information constitutes an admission that the drug caused or contributed to an adverse effect.").

56 *See* Daubert v. Merrell Dow Pharmaceuticals, Inc., 113 S. Ct. 2786, 2797 (1993) ("Publication is not a *sine qua non* of admissibility; it does not necessarily correlate with reliability, and in some instances, well-grounded but innovative theories will not have been published.") (citations omitted).

The supplementary disclosure should include unpublished studies or reports that raise important concerns that might influence an expert. An example of this type of unpublished information arises when a clinical investigator notes special problems with a drug. *See* White v. Wyeth Lab., Inc., 533 N.E.2d 748, 755 (Ohio 1988) (Douglas, J., dissenting in part and concurring in part) (taking note of defendant lab's internal memorandum that found level of risk from drug "unacceptable").

57 *See* Gibbs & Mackler, *supra* note 18, at 235 (explaining that the FDA maintains a list of over two hundred readily accessible publications, thus rendering it difficult for manufacturers to defeat a claim that the manufacturers "should have known" of an article printed in one of the listed publications). *See* Flannery, *supra* note 18, at 45-50, for some insight on reporting requirements for foreign adverse reactions.

effect within the categories of serious effects covered by FDA reporting requirements, e.g., fatal, life-impairing, long hospital stay, carcinogenic, or congenital abnormality.[58] The most recent reports would appear first within the categories.[59] Duplicative reports need not be included if they would not concern a reasonable physician in advising a reasonable patient.

The timing and updating of the supplementary disclosures present difficult issues: some patients may want very current reporting and if these patients become injured, they could assert that the non-inclusion of very recent studies in the listings affected their decisions about whether to take the drug. On the other hand, there can be costs in frequent labeling changes, and the reports may appear to be more significant than they actually are if immediate changes must be routinely made to cover every new study in journals covered by the listings. Overall, it would be desirable to provide the drug labeling with quarterly updates. The printed annual compilation might be updated by a "pocket part."[60] To deal with emergency situations, other forms of communication to physicians are more appropriate.[61]

V. Assessment of Supplementary Literature Digest

A. *Value of Supplementary Disclosure*

1. Patient Choice

The primary value of this supplementary disclosure would be to provide a means for physicians to consider emerging risks when advising their patients and to permit the patient the option to decline to undertake these risks, even though other reasonable physicians and experts might consider the risk reasonable, or that the risk had not been sufficiently established. The appropriateness of disclosing these debated risks arises from an estimate about what the reasonable patient expects when the risks from drugs cannot be fully determined.

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58 *See* 21 C.F.R. § 312.32 (1993). The type of effect should also be stated in parentheses in lay language if the supplementary disclosures are to be provided to patients.

59 To the extent the supplementary disclosures cover favorable and unfavorable reports concerning adverse reactions, the unfavorable reports should be printed in bold or in a manner that would set them off from the other disclosures.

60 21 C.F.R. § 312.32(d)(4) (1993) (prescribing that the results of follow-up investigations shall be submitted in information amendments or annual reports).

61 Cooper, *supra* note 12, at 238-39.

2. Accountability

The addition of these disclosures to the labeling has another advantage: it makes risk information that the FDA is still reviewing, but has not considered sufficient to warrant cautions and warnings, more accessible to physicians and the public. This type of widespread disclosure permits more debate and review within the medical community about the types of risks that generally need the most attention by physicians in prescribing drugs.

Doing so also makes the FDA itself more accountable. In the end, the public and scientific community's access to the supplementary information increases the weight the FDA decisions deserve. The decision regarding whether a risk is sufficiently important to warrant the need for a warning or a caution is a judgmental one. It can be a hard choice for anyone to make. The deference that the FDA deserves in making these decisions relates in part to its genuine and unparalleled expertise in applying "the most rigorous scientific standards . . . in the world."[62] But another important part of the due deference for agency decisions is the openness of the decision and the prospect of accountability. The process of accountability inevitably leads to a willingness to consider the other side of the question and to accept the possibility of changing decisions as more is learned.

Moreover, the review of drug use in tort suits has served a similar function because drug manufacturers must consider the need for disclosures that go beyond those required by the FDA. Opening up the decisions to scientific review on a contemporaneous basis provides another alternative means for some review and accountability.

3. Risk Avoidance and Value in Managed Care

Ready access to more information about a drug's risks may also be of use in avoiding unnecessary injury. When patients are suffering illnesses that their physician cannot diagnose, the physician might take a closer look at the supplementary disclosures about other adverse effects for the drug that the patient is taking.[63] In this manner, the physician might be able to spot warning signs

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62 Scarlett, *supra* note 9, at 33.

63 *See* Wooderson v. Ortho Pharmaceutical Corp., 681 P.2d 1038 (Kan.) (physician reported he would have stopped patient from using drug if he knew of possible association to renal failure, and might have earlier recognized adverse reactions to the drug), *cert. denied*, 469 U.S. 965-66 (1984).

of possible adverse reactions earlier than if the supplementary disclosures had not been made.

This additional information about emerging risk issues might also be of some special interest to health care providers in a managed care system. These providers may wish to take a more active role in evaluating the benefits and risks of drugs in promoting the overall health of patients.[64]

B. Drawbacks of a Supplementary Disclosure

A supplementary disclosure of emerging risks, as suggested here, is not without its complications.

1. Risks of Additional Litigation

Drug manufacturers may see the need to provide a supplementary literature digest as presenting the worst of options, because it may open up litigation about the adequacy of the disclosures made in the supplement. Moreover, it would eliminate the essence of the regulatory compliance defense. The fact that the FDA did not consider disclosure of the risk necessary in the FDA-reviewed list of warnings and cautions would not constitute a defense. The risk would have to be disclosed anyway, but in a different format.

The aim, of course, is different. The disclosures in the labeling of the risks recognized by the FDA along with the digest of literature reports of studies on other risks should lead courts to accept the disclosures as ordinarily sufficient to limit liability when an uncertain risk is realized. Regulatory compliance would be important with respect to the prominence to be given to risks. The only risks that would need to be displayed prominently would be those necessary to meet the regulatory standards set by the FDA. The supplementary disclosures would become a means of satisfying the manufacturer's duty to ensure patient access to other risk information.

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[64] An indirect indication of the relationship between information developed by managed care providers and drug effects is provided by Merck's recent acquisition of Medco. Published reports indicate that one of Merck's principal aims in pursuing the Medco takeover was Merck's desire to obtain access to effectiveness data compiled by Medco through its drug distribution programs. *See* Milt Freudenheim, *Merck's Big Gamble on a Merger*, N.Y. TIMES, Aug. 5, 1993, at D1, D2 ("Merck said it was seeking Medco's hoard of information about the 33 million drug customers in its managed-care plans. Merck plans to mine the data for patterns of medical effectiveness and use the information to increase sales."). These compilations might also provide information on adverse effect patterns.

2. Lack of Utility and Overload

The supplementary listing can be seen as contributing to information overload. The list might also be viewed as a useless exercise, imposing costs for complying but benefiting physicians and patients little, if at all.

The additional disclosures, of course, run some risk of adding to information overload. While the cure for information overload is not more information, the remedy can be found in putting the information in context. The supplementary format should provide a relevant context for evaluation. The continued prominence of the basic labeling reviewed by the FDA should provide the means for physicians to get the most important information. The digest format would provide access for those who wish to find out about additional risks whose significance is under study and review.

The compilation will also cost some additional resources, but the information already needs to be gathered and monitored by drug manufacturers to comply with FDA requirements. The printing costs should not be insurmountable.

3. Overdeterrence of Patients and Adequacy of Scientific Support

The listing of possible side effects may discourage some physicians and patients from using drugs. Most experts might view this as patient overreaction that inhibits the patients from using drugs that will produce beneficial effects.[65] Moreover, leading experts may regard some of the studies reported in the literature as being insufficiently supported.

At one level, this objection is a classic one, and, as discussed before, the consideration to be weighed against it is the patient's right to choose the manner and course of her treatment with guidance from the patient's physician.[66] The supplementary disclosure process presents an additional complication, though, because

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65 *Cf.* Lasagna, *supra* note 1, at 339 (reporting on what may be perceived as patients' overreaction to the dangers of the drug Bendectin, where studies of the drug may not actually prove that the drug is as dangerous as reported).

66 *Compare* Canterbury v. Spence, 464 F.2d 772 (D.C. Cir. 1972) (discussing the general notion that a patient must be given reasonable information in order to obtain informed consent to treatment) *with* Hippocrates, *Decorum*, (W.H.S. Jones trans. 1923), *in* ETHICS IN MEDICINE: HISTORICAL PERSPECTIVES AND CONTEMPORARY CONCERNS 8 (Stanley J. Reiser et al. eds., 1977) (explaining that Hippocrates counseled physicians to provide care with solicitude, "revealing nothing of the patients' future or present condition for many patients through this cause have taken a turn for the worse.") (footnotes omitted).

it would list studies chronologically. These studies may well have shortcomings and limitations, but the absence of some explanation of their deficiencies may make them appear more persuasive than warranted.

Physicians who read the listings are acquainted with the scientific process, and should have some ability to put the digest of literature studies in perspective, especially because the digest would be presented as a watch list of new reports, detailing drugs for which the FDA may not have considered changing their basic labelings. Moreover, other studies may be done on a continuing basis to respond to the concerns raised, and, as time progresses, these additional studies would be reflected in the digest.

Because of the time needed to do additional studies, though, the manufacturer should be permitted to include comments (after the reports of any study in the digest) that reflect differences in the evaluation of the scientific reliability and significance of the study. These comments should be based on the required study report that the manufacturer must file with the FDA.[67] Furthermore, the comments should not be misleading.

Of course, when appropriate, the FDA might also take an affirmative position in the basic drug labeling about the significance, or non-significance, of the reported studies. When the FDA does so, there would be an articulated, reasoned explanation for the consensus judgment about debated studies. In this way, the FDA will help promote a better and more informed understanding.[68]

The digest format would, however, still provide for the inclusion of studies that manufacturers and experts may regard as insufficient for establishing a drug risk. Leading experts, and even the consensus of opinion, may regard the studies as "junk science."

The exact meaning of "junk science" is itself debated. Under the Supreme Court's decision in *Daubert v. Merrell-Dow Pharmaceuticals, Inc.*, the litmus test in federal court litigation is not "general acceptance" by scientific experts, but the existence of relevant and reliable scientific evidence.[69] Under this standard, the digested

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[67] *See* 21 C.F.R. § 201.200 (1993) (providing for submission to the FDA of summaries of post-approval studies).

[68] Whether the FDA would need to review the supplementary digest in advance is a separate issue. The most suitable approach for review of the supplementary digest would involve the manufacturer issuing and revising the supplementary digest without prior review by the FDA, but with notice to the agency. Any disclosures reflecting on the adequacy of the FDA-provided labeling should be made, however, by submitting to the FDA a request for approval of a supplemental NDA.

[69] Daubert v. Merrell Dow Pharmaceuticals, Inc., 113 S. Ct. 2786 (1993). Publica-

studies would have to be based on accepted scientific techniques, and would ordinarily have been published in scientific journals, but they would not have to reflect the consensus of expert opinion. The very aim of the proposal is to include in the digest studies about emerging risks where experts differ in their evaluation. Access to that debate is, as suggested above, something to which physicians and reasonable patients should be given access. Moreover, the better way to resolve the worth of the debated studies is to provide access to them such that those affected can decide if they are concerned with risks beyond those clearly established, and to provide those at risk with references to additional information.

4. Effect on Medical Malpractice

The provision of supplementary risk information might be of concern to physicians who fear that they would face malpractice suits for not taking adequate account of the risks disclosed. Deviation from the FDA-approved labeling has been considered evidence of negligence in some instances.[70]

The inclusion of disclosures about additional risks in the supplementary labeling should not have an impact on the malpractice standards with respect to decisions to use a drug. The digest would not reflect FDA-recognized positions, and it should not carry any special weight in establishing the duty of care. The information would be available for the physician to take into account in exercising her best judgment about the care to be provided. The prevailing standard of care for determining malpractice should govern the extent to which that information needs to be considered by physicians generally with respect to the use of the drug.[71]

The supplementary digest could have some relevance, however, in judging the nature of the disclosures physicians should make to their patients to ensure informed consent to drug therapy. Courts continue to recognize that physicians have an obligation to inform their patients of drug risks, even though there is no obligation by the manufacturers to inform the patients directly.[72] The

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tion in a peer-reviewed publication is "relevant, though not dispositive" in judging reliability. *Id.* at 2797.

70 *See* Mulder v. Parke Davis & Co., 181 N.W.2d 882, 884-85 (1970); James R. Bird, Note, *Package Inserts for Prescription Drugs as Evidence in Medical Malpractice Suits*, 44 U. CHI. L. REV. 398, 400-05 (1977).

71 The extent to which President Clinton's 1993 Health Care Plan would change these standards is not considered here.

72 *See* Teresa M. Schwartz, *Consumer Warnings for Oral Contraceptives: A New Exception to the Prescription Drug Rule*, 41 FOOD DRUG COSM. L.J. 241 (1986) ("Until recently, courts uniformly have held that the duty of drug manufacturers to warn of risks associ-

physician can be held liable for failing to inform the patient of drug risks contained in the labeling, which is provided by the manufacturer to the physician.[73]

If physicians had to discuss with their patients each of the digest studies, the burdens and time demands could be considerable. One way to deal with this is to recognize that the aim is to inform patients that there is dispute among the experts. A disclosure need not be made of all the digest studies, so long as patients recognize that there is some dispute and have the opportunity to know more if they wish.[74]

5. Sufficiency of Information to Affect Liability

The supplement would provide only brief descriptions of the reports. Some may view the disclosures provided as an ineffective means of determining the adequacy of disclosures for purposes of determining liability. Nonetheless, the limited information contained in the supplement is consistent with the supplement's aim of providing access to major reports and issues concerning emerging and uncertain risks in an attempt to ensure patient choice. The matters covered would seem to be the more important and the more feasible to provide.

Moreover, providing the supplementary disclosures, and complying with warnings sought by the FDA, need not be the limit of the appropriate disclosures.[75] As a safeguard against the drawbacks of a regulatory compliance defense and regulatory capture, the ALI Reporters' Study proposed conditioning the defense on recognition of an obligation on the manufacturer to disclose to the agency when the manufacturer believes the agency's standards for disclosing risks are inadequate.[76] Similarly, drug manufacturers should also have an overriding obligation to disclose when the FDA standards for disclosure are, in the manufacturers view, inade-

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ated with prescription drugs runs only to physicians, and not to consumers.") (footnote omitted).

73 *See* Niemiera v. Schneider, 114 N.J. 550, 559, 662-67, 555 A.2d 1112, 1116, 1119-1121 (1989) (no duty of manufacturer to warn patient, but remand for trial on physician's duty to warn with court noting need to further patient's interest in autonomy). The standard for disclosure is information significant to a reasonable person, as determined by a jury, and is not to be governed by "bright line" guides about the need for statistical life expectancy data set by the courts. Arato v. Avedon, 858 P.2d 598, 606-07 (Cal. 1993).

74 *See infra* Part VI for a recommendation of patient labeling as a more direct way of providing patients with relevant information.

75 *See* II Reporters' Study, *supra* note 5, at 97-100.

76 *Id.* at 97, 100.

quate. Under the Reporters' Study, the necessary disclosures were made only to the FDA. A better approach would be to require the manufacturer to include, in a prominent manner, the scientific basis for the manufacturer's concerns about the need for more warnings in the supplementary digest.[77]

VI. PATIENT LABELING

If patient choice is an important concern for drug labeling, a further implication is that more should be done to provide the information directly to the patient. Drug manufacturers now provide the risk information to the physician, and it is the physician who acts as a learned intermediary in providing the disclosures to the patient. For the most part, the drug manufacturer has no regulatory duty, or tort obligation, to ensure that written information is provided to the patient.[78]

While the FDA has recognized the value of patient labeling, in the past the agency withdrew its regulatory initiative in favor of voluntary efforts that would provide the labeling in a better manner. Some, myself included, have some skepticism about whether physician disclosures or the other alternatives are as reliable in reaching the patient as written patient labeling provided with the drug when dispensed.[79] Thus, as a policy matter, a renewal by the FDA of an effort to require patient labeling on prescription drugs would be a welcome development.

In the absence of a general requirement for patient labeling, attention should continue to be given to situations that especially warrant assurances of patient access to information. Labeling for patients seems particularly important for innovative drugs. Innovative drugs, in their immediate Phase IV marketing, present a distinct possibility for posing additional adverse effects, discoverable

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77 Moreover, regulatory compliance, accompanied by the supplementary disclosures, can still be regarded as establishing a presumptive rather than a conclusive defense. A conclusive defense would, of course, be more conducive to guarding against liability costs that would impact on innovation. On the other hand, a presumptive defense is more suitable to the incremental growth of the law. Change is also more acceptable when it leaves some leeway to the courts to deal with consequences not fully anticipated.

78 *See* Schwartz, *supra* note 72, at 241 (explaining that drug manufacturers have traditionally been viewed as having no duty to disclose to consumers the risks associated with drugs, but that the manufacturers nonetheless had a duty to disclose such risks to physicians).

79 *See generally* Margaret Gilhooley, *Learned Intermediaries, Prescription Drugs, and Patient Information*, 30 ST. LOUIS U. L.J. 433 (1984). *See also* Rosalind M. Kendellen, *The Food and Drug Administration Retreats from Patient Package Inserts for Prescription Drugs*, 40 FOOD DRUG COSM. L.J. 172, 177 (1985).

only by the general public's use of the drug. This Phase IV is similar to a continuation of experimental testing.

The appropriateness of informed consent for experimental testing is generally acknowledged.[80] Obtaining that consent usually involves written disclosures, in addition to oral discussions. In a similar way, information should be given to users of Phase IV drugs about the known risks of the drug, and the patient should have access to any additional risks identified in current research, even when the assessment of the risks is still in progress. The patient labeling would identify its focus on the principal risks for which clear evidence exists, but should also provide the patient with a copy of the supplementary digest as a source of additional information to consider in consultation with her physician.

VII. CONCLUSION

In deciding whether regulatory compliance should preclude tort liability it is important to consider not only the adequacy of disclosures to physicians about information the physician needs in making treatment decisions, but also the adequacy of disclosures needed to enable the physician to inform patients about risks that concern patients. The patient's interest in informed consent is an important value to be protected in its own right. As suggested here, reasonable patients may want access to information about risks that are debated among experts even when the risk may not be clearly enough established that disclosure would necessarily be required under the FDA's regulatory criteria. One way of safeguarding patient choice would be to include a supplementary digest of current literature studies about risks that may be associated with a drug, along with the drug labeling ordinarily provided to physicians. This provision of supplementary disclosures may not be the only way of safeguarding the patient's interest in informed consent. The present tort system also works to protect this interest by identifying risks selectively and retrospectively, in particular cases, when injury occurs, that should have been disclosed by a reasonable manufacturer. Uncertain as that standard is, it serves to encourage attention to the additional warnings that reasonable physicians and patients may want. Before the tort standards are changed to limit the scope of the warnings provided for pharmaceuticals, adequate attention needs to be given to whether the change will adequately safeguard patient choice.

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[80] *See supra* note 54 for a short discussion on informed consent.