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## Failure-to-Warn: Facing up to the Real Impact of Pharmaceutical Marketing on the Physician's Decision to Prescribe

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## **FAILURE-TO-WARN: FACING UP TO THE REAL IMPACT OF PHARMACEUTICAL MARKETING ON THE PHYSICIAN’S DECISION TO PRESCRIBE**

Katherine T. Vukadin\*

ABSTRACT .....	76
INTRODUCTION .....	77
I. PHARMACEUTICAL MARKETING: AN EXPENSIVE ENDEAVOR THAT RELIABLY AFFECTS PRESCRIBING DECISIONS .....	78
A. Pharmaceutical Companies use Social Psychology to Create a Relationship that Influences Physicians at the Subconscious Level ...	79
1. Pharmaceutical Marketing is Grounded in Social Science Research.....	80
2. Pharmaceutical Marketing Results in no Increase in Prescribing Quality—Only a Decrease in Prescribing Quality and Increases in Cost.....	83
B. Pharmaceutical Representatives Offer Carefully Selected Information that Often Downplays the Documented Risks .....	84
II. A HOST OF REGULATIONS AND NEW ETHICS INITIATIVES DO NOT DECREASE AGGRESSIVE MARKETING AND ANTI-WARNINGS .....	88
A. Extensive Regulations Apply to Pharmaceutical Labeling and Promotional Materials.....	88
B. Promotion and Advertising are Regulated .....	90
C. Self-Policing and Ethics Policies have made some Inroads but Remain Incomplete .....	91
D. FDA’s Collaborative Approach to Enforcement Leaves Gaps for Non- Compliance .....	93
III. COURTS SHOULD CONSIDER BOTH WARNINGS AND ANTI-WARNINGS .....	95

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A. Failure-To-Warn Liability Turns on the Presence of a “Reasonable” Warning .....	95
B. The Package Insert Should not be the Sole Focus.....	97
1. Focus on the Package Insert Ignores the Warning-Diluting Information that Reaches Physicians through Pharmaceutical Marketing.....	97
2. Information about Pharmaceuticals is Dynamic While the Package Insert is Slow to Change.....	101
3. While the Package Insert is Easily Available, Marketing Information is Often Unavailable as Evidence.....	101
4. Exclusive Focus on the Package Insert Elevates the Regulations to De Facto Preemptive Status.....	102
C. The “Overpromotion” Exception to the Learned Intermediary Defense is Inadequate, Because the Bar is Impossibly High .....	104
IV. TOTAL MIX: THE FAILURE-TO-WARN ANALYSIS SHOULD CONSIDER ALL OF THE PHARMACEUTICAL COMPANY’S WARNING AND WARNING-DILUTING INFORMATION .....	106
A. Courts Analyzing the Reasonableness of a Warning Should Consider the Full Spectrum of Warning and Anti-Warning Information that Reaches Physicians—Not Just the Package Insert .....	106
B. In the Causation Analysis, a Physician’s Failure to Read the Package Insert Alone Should not be Sufficient to Defeat Causation .....	109
C. Social Psychology-Based Marketing Operates at a Subconscious Level, so a Physician’s Own Statement on its Effects Should not be Conclusive as to the Causation Element .....	110
V. CONCLUSION .....	111

“It’s my job to figure out what a physician’s price is . . . at the most basic level, everything is for sale and everything is an exchange.”<sup>1</sup>

#### ABSTRACT

*Pharmaceutical side effects cause more than 100,000 deaths per year.<sup>2</sup> Because pharmaceuticals pose serious risks, the Food and Drug Administration carefully vets the written warnings that physicians receive about each drug. But alongside these official warnings, attractive pharmaceutical representatives offer slick sales pitches in what amounts to a multi-billion-dollar campaign aimed at influencing the physician’s judgment.*

*Pharmaceutical representatives are known to downplay the package insert’s warnings. Based on social science research, the marketing operates at a subconscious level, so*

1. Shahram Ahari & Adriane Fugh-Berman, *Following the Script: How Drug Reps Make Friends & Influence Doctors*, PLOS MED (Apr. 24, 2007), <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1876413/>. Mr. Ahari is a former pharmaceutical representative for Eli Lilly.

2. *Preventable Adverse Drug Reactions*, FOOD & DRUG ADMINISTRATION, <http://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/druginteractionslabeling/ucm110632.htm#ADRs>: Prevalence and Incidence (last visited Aug. 6, 2013).

*targeted physicians are often unaware of its surreptitious effects. Nonetheless, pharmaceutical company defendants in failure-to-warn lawsuits can often obtain summary judgment based purely on the package insert, while the pervasive—and effective—warning-diluting marketing information is ignored.*

*This article proposes that the failure-to-warn inquiry face up to pharmaceutical marketing's potent role in many prescribing decisions. Courts assessing a warning's adequacy cannot stop at the package insert but must consider the warning-diluting marketing information as well. And when causation is the question, the physician's testimony should not be conclusive as to the marketing information's effects. Failure-to-warn jurisprudence should stop relying on empty paper compliance and recognize present-day pharmaceutical marketing as a compelling and driving force in the decision to prescribe.*

#### INTRODUCTION

Pharmaceuticals cure disease and prolong life. Their side effects, however, cause more than 100,000 deaths per year.<sup>3</sup> Pharmaceuticals are aptly recognized as “inherently dangerous” products that require special care in their use. Given these risks—and patients’ reliance on physicians’ judgment in prescribing pharmaceuticals—the warnings and marketing materials reaching physicians should be carefully regulated. In some respects, they are. The package insert accompanying each pharmaceutical is carefully vetted by the federal Food and Drug Administration. In a failure-to-warn lawsuit, this insert is decisive; a pharmaceutical company defendant can most often brandish the package insert and cut off liability via summary judgment.

But another, perhaps more influential, source of information reliably reaches physicians. Pharmaceutical representatives’ slick sales pitches to physicians amount to a billion-dollar campaign that can eclipse the lengthy written package insert whose minute text tends to remain unread. Unlike the colorless package insert, pharmaceutical representatives offer an alluring message often delivered by attractive individuals culled from the ranks of college cheerleading squads.<sup>4</sup> Pharmaceutical representatives make about 115 million physician sales calls per year.<sup>5</sup> Documents obtained in litigation and first-hand accounts show pharmaceutical representatives downplaying the very warnings described in the package insert. Nonetheless, pharmaceutical companies in failure-to-warn lawsuits are

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3. *Id.*

4. Reuters, *U.S. Files 2nd Suit Accusing Novartis of Kickbacks to Doctors*, N.Y. TIMES, Apr. 26, 2013, at B8. According to the lawsuit, Novartis paid rich speaking fees to physicians for over a decade and provided lavish meals including one at the restaurant Nobu that cost over \$10,000, all as an inducement to prescribe Novartis’s drugs. The government also alleges that the incentive program led to the Medicare and Medicaid programs’ paying “millions of dollars in reimbursements based on kickback-tainted claims for medication like the hypertension drugs Lotrel and Valturna and the diabetes drug Starlix,” *Id.* Pharmaceutical companies frequently recruit directly from college cheerleading squads, monitoring which cheerleaders are graduating and targeting specific cheerleading programs. Stephanie Saul, *Gimme an Rx! Cheerleaders Pep Up Drug Sales*, N.Y. TIMES, Nov. 28, 2005, at A1 (“Anyone who has seen the parade of sales representatives through a doctor’s waiting room has probably noticed that they are frequently female and invariably good looking. Less recognized is the fact that a good many are recruited from the cheerleading ranks.”). Pharmaceutical company managers respond that cheerleaders are hired for personality rather than looks, *Id.* (““Obviously, people hired for the work have to be extroverts, a good conversationalist, a pleasant person to talk to; but that has nothing to do with looks, it’s the personality,” said Lamberto Andreotti, the president of worldwide pharmaceuticals for Bristol-Myers Squibb.”).

5. Jonathan D. Rockoff, *Drug Sales Reps Try a Softer Pitch Physicians – In Changed Times, Physicians Increasingly Set Agenda*, WALL ST. J., Jan. 10, 2012, at B1.

usually able to obtain summary judgment based purely on a package insert, while the overwhelming and effective warning-diluting marketing information is ignored.

This article proposes that the failure-to-warn inquiry recognize pharmaceutical marketing's central role in many prescribing decisions. Pharmaceutical marketing downplays warnings, making the package insert less effective. This means that when courts decide the adequacy of a warning, as the initial step in a failure-to-warn claim, a realistic assessment of the "warning" should include not only the package insert, but also the marketing information that reaches physicians far more reliably than the package insert. In addition, pharmaceutical marketing affects the second step in the failure-to-warn analysis, namely whether an inadequate warning actually caused the plaintiff's injury. At present, pharmaceutical companies commonly escape liability on summary judgment, when physicians testify that pharmaceutical companies' statements did not affect them, and a better warning would have made no difference. But pharmaceutical marketing, based on painstaking social science research, operates at a subconscious level—the physician-target is the person least able to testify to its effects. Both the warning adequacy and causation issues, therefore, should be left for the jury's consideration. Pharmaceutical companies should be fully accountable for their marketing to physicians. Particularly because pharmaceutical companies are legally required to warn only physicians and not patients, the total mix of information that physicians receive must be considered in any failure-to-warn case, and a jury should decide causation.

Part I of the article shows how pharmaceutical companies' marketing techniques surreptitiously affect physicians' prescribing habits. Part II explains why the existing web of pharmaceutical regulations and policies is ineffective in curbing pharmaceutical sales practices. Part III shows the primacy of the package insert in failure-to-warn cases, together with some courts' consistent but frustrated desire to take pharmaceutical representatives' statements into account in failure-to-warn cases. Part IV explains that these realities of pharmaceutical marketing require that the failure-to-warn inquiry adapt in the following ways: (1) the warning at issue should include not just the package insert, but also marketing information; (2) a physician's failure to read the package insert should not alone be sufficient to defeat causation; and (3) a physician's own statement as to a lack of reliance on the pharmaceutical company's information should not defeat causation.

#### I. PHARMACEUTICAL MARKETING: AN EXPENSIVE ENDEAVOR THAT RELIABLY AFFECTS PRESCRIBING DECISIONS

Pharmaceutical marketing is a multi-billion-dollar industry that has a well-documented influence on physicians' prescribing choices and habits. Pharmaceutical marketing expenditures in the United States exceeded \$27 billion in 2012.<sup>6</sup> Some estimate that pharmaceutical companies spend about two times as much money on marketing than they do on research and development; approximately 24.4 percent of each revenue dollar is spent on marketing, as opposed to 13.4 percent on research and development.<sup>7</sup>

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6. 2012 *U.S. Pharmaceutical Promotion Spending*, CEGEDIM STRATEGIC DATA, (Jan. 2013), [http://www.skainfo.com/health\\_care\\_market\\_reports/2012\\_promotional\\_spending.pdf](http://www.skainfo.com/health_care_market_reports/2012_promotional_spending.pdf).

7. Donald W. Light & Joel R. Lexchin, *Pharmaceutical Research & Development: What Do We Get for All*

The pharmaceutical industry considers detailing—physician-directed marketing—to be the most effective form of pharmaceutical marketing.<sup>8</sup> Pharmaceutical sales representatives pay about 115 million visits to 340,000 doctors each year.<sup>9</sup>

A. *Pharmaceutical Companies use Social Psychology to Create a Relationship that Influences Physicians at the Subconscious Level*

The most crucial aspect of pharmaceutical representatives' marketing to physicians is the representative-physician relationship.<sup>10</sup> This relationship is based first on careful research on the particular physician's prescribing habits and patient behaviors. Pharmaceutical companies pay to find out which drugs a physician is prescribing and whether the patients are having prescriptions filled.<sup>11</sup> This information is readily available and trackable,<sup>12</sup> together with information on patients' medical conditions, lab results, and sometimes, demographic information.<sup>13</sup> One research firm has tracked information on doctors' prescribing habits since the 1990s—the available information now includes insurance claims data as well.<sup>14</sup> By tracking patient behavior data, together with prescribing information, research companies aim to give pharmaceutical representatives “the ability to understand not only the doctor's behavior, and which other physicians are key opinion leaders that the doctor listens to, but also the behavior of the doctor's patients.”<sup>15</sup>

The pharmaceutical industry closely monitors all contacts with physicians.<sup>16</sup> One

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*That Money*, THE BMJ, <http://www.bmj.com/content/345/bmj.e4348> (last visited Aug. 7, 2013).

8. Kanika Johar, *An Insider's Perspective: Defense of the Pharmaceutical Industry's Marketing Practices*, 76 ALB. L. REV. 299, 309 (2013) (citing SHAILI JAIN, UNDERSTANDING PHYSICIAN-PHARMACEUTICAL INDUSTRY INTERACTIONS 59 n.1 (2007)).

9. Rockoff, *supra* note 5.

10. *Id.*

11. Katie Thomas, *Data Trove on Doctors Guides Drug Company Pitches*, N.Y. TIMES, May 17, 2013, at B1 (“I think the doctors tend not to be aware of the depths to which they are being analyzed and studied by the people trying to sell them drugs and other medical products . . . . Almost by definition, a lot of this stuff happens under the radar—there may be a sales pitch, but the doctor may not know that sales pitch is being informed by their own prescribing patterns.”) (quoting Dr. Jerry Avorn, professor of medicine at Harvard Medical School and developer of programs to resist pharmaceutical marketing).

12. Pharmacies receive prescriber-identifying information on a routine basis when filling prescriptions, *Sorrell v. IMS Health, Inc.*, U.S., 131 S. Ct. 2653, 2659 (2011). Many pharmacies sell this information to “data miners,” companies that analyze and report on this information; pharmaceutical companies in turn pay for access to these reports, so their marketing efforts can be more closely tailored to a particular prescriber's habits and preferences. *Id.* at 2660. The United States Supreme Court recently struck down a Vermont law making such sales of prescriber practice information illegal, on the basis that the law was an unconstitutional burden on protected speech. *Id.* at 2659.

13. *Id.*

14. *Id.*

15. Thomas, *supra* note 11 (quoting Jerry Maynor, the director of marketing for North America at Cegedim Strategic Data).

16. *The Doctor Won't See You (Mr. Pharma Rep), Now; Number of 'rep-accessible' docs falls another 20 percent; 'rep-inaccessible' docs increase 50 percent*, PR NEWSWIRE, May 6, 2012. Pharmaceutical companies can subscribe, for example, to services such as AccessMonitor, described as “a proprietary tool that incorporates the call reports from more than 200 different U.S. pharmaceutical sales teams representing more than 175 different products. The report equips companies with data to make the best use of sales and marketing resources in a systematic way and includes sales operations, field management and marketing strategies. *Id.* This could involve making meaningful changes to sales force structure and deployment, improving territory and compensation plan design, and analyzing marketing effectiveness and use of alternative media. The data supplied by the AccessMonitor™ report enables each pharmaceutical company to determine its own response to the current environment “based on its unique needs.” *Id.* Pharmaceutical companies use information on which prescribers are already

service counts the number of visits by pharmaceutical representatives and ranks physicians based on their willingness to see pharmaceutical representatives: completely open, sometimes willing to see pharmaceutical representatives, or completely unwilling.<sup>17</sup>

### 1. Pharmaceutical Marketing is Grounded in Social Science Research.

Based on the data they study, pharmaceutical representatives forge a relationship that goes on to influence physicians at the subconscious level. Pharmaceutical representatives are trained in human behavior, and they studiously build and attend to their relationships with physicians. For example, representatives study physicians' offices to see if there is any kind of trinket or photograph that can serve as the springboard to a personal connection.<sup>18</sup> They share meals to promote bonding and sharing behaviors, in which the representative behaves as a friend to the physician.<sup>19</sup> Pharmaceutical representatives also give gifts and arrange for payments, such as honoraria for speaking.<sup>20</sup> According to some studies, physicians have a "mostly negative" attitude toward the practice of pharmaceutical representatives providing gifts; however, the studies also report that such gifts "induce reciprocal feelings among physicians."<sup>21</sup>

Physicians themselves report that contacts with pharmaceutical representatives have little or no effect on their prescribing habits, although some believe that their colleagues' judgment may be affected.<sup>22</sup> When physicians say that pharmaceutical marketing plays only a minor role in their prescribing decisions, pharmaceutical companies tout this self-reporting as "evidence" that pharmaceutical marketing does no harm.<sup>23</sup> Significantly, however, physicians who meet with the greatest number of pharmaceutical representatives are the least likely to believe that their judgment would be affected.<sup>24</sup>

It is unsurprising, however, that physicians would report that they are not influenced or influenced by marketing, because pharmaceutical marketing uses principles of social

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using a drug, which turn to a competing drug, and how long a patient stays on a particular drug. David Orentlicher, *The Effects of Health Information Technology on the Physician-Patient Relationship*, 38 J.L. MED. & ETHICS 74, 75 (2010). While patient names are not disclosed, each patient is given a number, so that pharmaceutical companies can analyze the prescriptions for each patient as a whole. *Id.*

17. Orentlicher, *supra* note 16, at 75.

18. Ahari & Fugh-Berman, *supra* note 1 ("Reps scour a doctor's office for objects—a tennis racquet, Russian novels, seventies rock music, fashion magazines, travel mementos, or cultural or religious symbols—that can be used to establish a personal connection with the doctor.").

19. *Id.* ("During training, I was told, when you're out to dinner with a doctor, 'The physician is eating with a friend. You are eating with a client.'").

20. *Id.*

21. Puneet Manchanda & Elisabeth Honka, *The Effects and Role of Direct-to-Physician Marketing in the Pharmaceutical Industry: An Integrative Review*, 5 YALE J. HEALTH POL'Y L. & ETHICS 785, 809 (2005); see also Jason Dana & George Loewenstein, *A Social Science Perspective on Gifts to Physicians from Industry*, 290 J. AM. MED. ASS'N 252, 252-54 (2003).

22. M.A. Morgan et al., *Interactions of Doctors with the Pharmaceutical Industry*, 32 J. MED. ETHICS 559-63 (2006).

23. *Pharmaceutical Marketing in Perspective: Its Value and Role as One of Many Factors Informing Prescribing*, PHARMA, available at [http://phrma.org/sites/default/files/pdf/phrma\\_marketing\\_brochure\\_influences\\_on\\_prescribing\\_final.pdf](http://phrma.org/sites/default/files/pdf/phrma_marketing_brochure_influences_on_prescribing_final.pdf) (last visited Nov. 8, 2013) (noting that only 14 percent of physicians report that pharmaceutical representatives have a "major" impact on prescribing decisions and that only eleven percent of physicians surveyed said that they consider information from pharmaceutical representatives a "great deal" as a factor in prescribing).

24. Brian Hodges MD, FRCPC, *Interactions with the Pharmaceutical Industry: Experiences and Attitudes of Psychiatry Residents, Interns, and Clerks*, 153 CAN. MED. ASS'N J. 553, 557 (1995).

psychology, which operate at a sub-conscious level.<sup>25</sup> Above all, pharmaceutical representative training emphasizes the importance of relationships: “[G]aining access and building relationships . . . are key to providing you the opportunity to influence your customers’ behaviors.”<sup>26</sup> Once the representatives have established a relationship, they can exert various and, subtle forms of social pressure to extract the result they seek. These pressures—based on well-known principles of social psychology—include “reciprocation, commitment, social proof, liking, authority, and scarcity.”<sup>27</sup> Representatives learn how to recognize physician receptiveness, and representatives study each of the potential roadblocks to physicians’ accepting the representative’s message and the means of overcoming each obstacle.<sup>28</sup>

Empirical evidence indicates that despite physicians’ beliefs to the contrary, pharmaceutical marketing is effective in influencing physicians’ actions, whether those actions result in requesting additions to a formulary, initiating use of a certain drug, or choosing to prescribe one drug over another.<sup>29</sup> Marketing changes physicians’ behavior, therefore,

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25. Sunita Sah & Adriane Fugh-Berman, *Physicians Under the Influence: Social Psychology & Industry Marketing Strategies*, 41 J. LAW, MED. & ETHICS 665 (2013) (noting that “[p]hysicians fail to recognize their vulnerability to commercial influences due to self-serving bias . . . even the most conscious and genuine commitment to ethical behavior cannot eliminate unintentional, subconscious bias”).

26. Memorandum from Rep. Henry A. Waxman, to the Democratic Members of the Government Reform Committee (May 5, 2005), available at <http://oversight-archive.waxman.house.gov/documents/20050505114932-41272.pdf>.

27. Sah & Fugh-Berman, *supra* note 25, at 665. Reciprocation is the principle that help or gifts should be reciprocal—pharmaceutical representatives therefore give gifts so as to prompt physicians to respond in kind. *Id.* at 667-68. Even small gifts result in feelings of reciprocity. *Id.* Commitment is the sense that one should abide by one’s promises. *Id.* Pharmaceutical representatives illicit feelings of commitment by overtly asking physicians to commit to selecting the marketed drug for the physician’s next few prescriptions. Social proof is the idea that one decides what to do by observing what others do; promotional items for a particular drug can increase physicians’ positive views of a particular drug. Liking or rapport increases with more frequent interactions and length of time of the relationship. *Id.* at 669 (noting that Jordan Katz, a former pharmaceutical sales representative, reported that “a lot of doctors just write [prescriptions] for who they like.”). Authority and scarcity involves pharmaceutical companies’ payments to “Key Opinion Leaders” to champion a particular drug. *Id.* Perhaps most significantly, these forms of influence operate largely on the subconscious, resulting in influence without physicians’ self-reporting or even realizing that they are so influenced. *Id.* at 665.

28. Sah & Fugh-Berman, *supra* note 25, at 665. Another important technique emphasized in Merck’s internal document entitled “Champion Selling” was to assess the personality of doctors in order to determine what type of information would be most convincing to them. For a doctor with a “technical” personality, sales representatives were taught to “use figures, percentages” in their pitches; for a doctor with a “supportive personality,” representatives were advised to “focus on benefits to patients”; and for a doctor with an “expressive personality,” representatives were told to “show enthusiasm; appeal to his/her ego.” Merck, *Champion Selling: Milestone Leader’s Guide* (Jan. 2002) (cited in Memorandum from Rep. Henry A. Waxman, *supra* note 26).

29. Mary-Margaret Chren & Seth Landefeld, *Physicians’ Behavior and Their Interactions with Drug Companies. A Controlled Study of Physicians who Requested Additions to a Hospital Drug Formulary*, 271 J. AM. MED. ASS’N 684, 684-88 (1994). In addition, numerous studies have asked physicians to report changes in their own behavior in response to pharmaceutical representatives’ contacts or gifts. In one study, almost a third of medical residents reported changing their own behavior in response to interactions with pharmaceutical representatives. Nicole Lurie, MD, MSPH, et al., *Pharmaceutical Representatives in Academic Medical Centers; Interaction with Faculty and Housestaff*, 5 J. GEN. INTERN. MED. 240 (1990). Another study examined objective information to determine the effect of pharmaceutical representatives’ contacts with medical residents. Mary-Margaret Chren & Seth Landefeld, *Physicians’ Behavior and Their Interactions with Drug Companies. A Controlled Study of Physicians who Requested Additions to a Hospital Drug Formulary*, 271 JAMA 684, 684-88 (Mar. 2, 1994). That study found that residents were more likely to initiate use of the company’s product within twelve weeks after contact with a representative. *Id.* See also Roger W. Spingarn, MD, Jesse A. Berlin, ScD, & Briam L. Strom, MD, MPH, *When Pharmaceutical Manufacturers’ Employees Present Grand Rounds, What Do Residents Remember?* 71 ACAD MED. 86 (1996) (finding that residents who attended a Grand Rounds presentation on the Lyme disease drug were more likely to recommend it as a first-line drug when it was indicated, and even when it was not).



despite the fact that modern medicine aims for prescribing decisions to be scientific and evidence-based.<sup>30</sup> Marketing, other than the distribution of even-handed studies, arguably stands in the way of unbiased medical decision-making.<sup>31</sup> Studies conclude that visits with pharmaceutical representatives have “a significant effect on physician prescription behavior.”<sup>32</sup>

Pharmaceutical companies’ spending on marketing is highly effective, although few studies to establish this have been funded.<sup>33</sup> Physicians exposed to pharmaceutical products through the provision of free samples, for example, are more likely to prescribe those medications and are less likely to use inexpensive alternatives.<sup>34</sup> Pharmaceutical companies refer to these samples as “starters,” because the purpose of them is to start the patient on a particular medication.<sup>35</sup> In addition, physicians who attend promotional events are documented as increasing their prescribing of the promoted medication.<sup>36</sup> One meta-analysis indicated that of twenty-nine studies of pharmaceutical representative visits, seventeen found an association with an increase in the prescribing of the marketed drug.<sup>37</sup> None of the studies found an absence of association between visits and increased prescribing.<sup>38</sup> Longer pharmaceutical representative visits were more likely to be associated with increased prescribing.<sup>39</sup> In addition, pharmaceutical representative visits mean more money spent on medicines: of eight studies, seven found that prescription costs increased with greater contact from pharmaceutical representatives.<sup>40</sup>

Where a drug shows no documented benefit over another, high levels of marketing can result in sales far exceeding the equivalent generic. For example, the blood pressure drug Bystolic, manufactured by Forest Laboratories, is a brand-name drug costing about eighty dollars per month, versus ten dollars per month for generic equivalents.<sup>41</sup> Upon Bystolic’s launch, Forest received a warning letter from the FDA stating that Forest had downplayed the serious risks of side effects, and had made unsubstantiated claims of superiority; indeed, the FDA stated that despite Bystolic’s claims of novelty and superiority,

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30. BEN GOLDACRE, *BAD PHARMA* 246 (2013).

The scale of this spend is fascinating in itself, when you put it in the context of what we all expect from evidence-based medicine, which is that people will simply use the best treatment for the patient . . . . In medicine, brand identities are irrelevant, and there’s a factual objective answer to whether one drug is the most likely to improve a patient’s pain, suffering and longevity. Marketing, therefore, exists for no reason other than to pervert evidence-based decision-making medicine.

*Id.*

31. *Id.*

32. Manchanda & Honka, *supra* note 21, at 809 (“While there seems to be little consensus about the size of the effect, it is clear that the effect is positive and significant in a statistical sense.”).

33. Geoffrey Spurling et al., *Information from Pharmaceutical Companies and the Quality, Quantity, and Cost of Physicians’ Prescribing: A Systematic Review*, PLOS MED (Oct. 19, 2010), <http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000352>.

34. Richard F. Adair & Leah R. Holmgren, *Do Drug Samples Influence Resident Prescribing Behavior? A Randomized Trial*, 118 AM. J. MED. 881 (2005).

35. Johar, *supra* note 8, at 312.

36. Spurling et. al., *supra* note 33, at 3.

37. *Id.* at 4.

38. *Id.*

39. *Id.*

40. *Id.* at 5.

41. Charles Ornstein et al., *Have You Ever Tried to Sell a New Drug?*, THE ATLANTIC (June 13, 2013), available at <http://www.theatlantic.com/health/archive/2013/06/have-you-ever-tried-to-sell-a-new-drug/277204/>.

the FDA was not aware of “any well-designed studies comparing Bystolic to other beta-blockers.”<sup>42</sup> Forest, however, undertook a “promotional assault,” deploying large numbers of pharmaceutical representatives to visit physicians and paying speaker fees to physicians who would speak about Bystolic.<sup>43</sup> Despite the lack of documented superiority over cheaper generic equivalents, Bystolic sold well.<sup>44</sup> Of the twenty top Bystolic prescribers in the Medicare prescription drug program, seventeen had financial ties to Forest, such as the payment of speaker fees.<sup>45</sup> The same is true for other drugs.<sup>46</sup> Explicit causal links between marketing and prescribing are naturally elusive, but according to some, “the evidence overwhelmingly suggests that doctors are influenced.”<sup>47</sup> To some physicians, the high sales of Bystolic were bewildering due to the lack of scientific evidence favoring the more expensive drug.<sup>48</sup>

## 2. Pharmaceutical Marketing Results in no Increase in Prescribing Quality—Only a Decrease in Prescribing Quality and Increases in Cost

Do pharmaceutical representative visits cause physicians to overlook or discount warnings, or to prescribe inappropriate medications? A few studies have tried to answer this question, using prescribing “quality”—measured by guideline adherence, prescribing appropriateness of a drug class, and prescribing range.<sup>49</sup> In one study, learning about a drug first from a pharmaceutical representative was associated with lower prescribing quality, whereas the number of representative visits was not associated with lower prescribing quality.<sup>50</sup> Another study showed an association between self-reported rates of attendance at pharmaceutical company-sponsored meetings and slightly lower quality scores, but not with self-reported rates of representatives’ visits.<sup>51</sup> And, with regard to adherence to prescribing guidelines, one study indicated that more frequent pharmaceutical representative visits were associated with less guideline adherence, while one showed no effect.<sup>52</sup> Neither study, however, showed an increase in guideline adherence with increased pharmaceutical visits.

Significantly, while pharmaceutical companies maintain that pharmaceutical representatives provide useful information to physicians, studies do not bear this out. Studies do not show that an increase in pharmaceutical representative visits corresponded with any

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42. Warning Letter from FDA to Howard Solomon, CEO of Forest Laboratories (Aug. 28, 2008), *available at* <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivities-byFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm054010.pdf>.

43. Ornstein et. al., *supra* note 41.

44. *Id.* (noting that Bystolic almost doubled its sales to \$348 million after the intense marketing efforts).

45. *Id.*

46. *Id.* (“For example, nine of the top prescribers of the Alzheimers drug Exelon received money from Novartis, the drug maker. Eight of the top 10 for Johnson & Johnson painkiller Nucynta were paid speakers, as were six of the top ten for Pfizer’s antidepressant Pristiq.”).

47. *Id.*

48. *Id.* (“I’ve no idea how you could come up with a storyline for use of that drug,” noted Eric Topol, a cardiologist and chief academic officer of Scripps Health. “I don’t see any purpose for Bystolic whatsoever.”).

49. Spurling et al, *supra* note 33 at 2.

50. *Id.* at 3.

51. *Id.*

52. *Id.*

increase at all in prescribing quality.<sup>53</sup> Indeed, the only effect documented was the opposite. This lack of benefit—and documented downside—suggests that pharmaceutical representatives' visits to physicians are having too great an effect and marketing has been allowed to go too far, as pharmaceutical representatives' visits cause a documented downside with no documented upside.<sup>54</sup>

*B. Pharmaceutical Representatives Offer Carefully Selected Information that Often Downplays the Documented Risks*

First-hand accounts and FDA documents show repeated instances of pharmaceutical representatives presenting one-sided information that downplays risks and negates warnings.<sup>55</sup> Because many of these interactions occur in private conversations, there is little empirical data to indicate how frequently warnings are downplayed or negated by marketing activities. The overall picture, however, can be pieced together from information from physicians themselves, from retired pharmaceutical representatives, and from documents released in litigation. Together, these sources indicate that risks are downplayed all too frequently.

As described in more detail below, every pharmaceutical approved by the FDA must have “labeling” that contains the risks and warnings pertinent to that pharmaceutical.<sup>56</sup> The labeling contains the complete prescribing and warning information that must be included as a package insert for the pharmaceutical.<sup>57</sup>

But the pharmaceutical representative's oral description of a drug in the physician's office is often a highly selective version of the complete warning information that appears in the label.<sup>58</sup> Pharmaceutical representatives may, for example, present studies that support one safety profile while ignoring those that show greater risks, deny that the written warnings are a concern, or simply omit warnings.<sup>59</sup>

53. *Id.* Under certain circumstances, though, pharmaceutical marketing could have positive public health results. In the case of Herceptin, for example, a 2005 study showed that the drug could cut the relapse rate of early stage tumors in half. Scott Gottlieb, *From FDA, A Good Framework for Distributing Information on Off-Label Uses*, HEALTH AFFAIRS BLOG (Apr. 23, 2008), <http://healthaffairs.org/blog/2008/04/23/from-fda-a-good-framework-for-distributing-information-on-off-label-uses/>. FDA approval of the drug for this use came two years after the study's results; in the meantime, physicians were slow to embrace the drug for this use. *Id.* There is a case to be made, therefore, that certain limited distribution of study results could have positive effects for patients. *Id.*

54. David Henry, *Doctors and Drug Companies: Still Cozy After All These Years*, PLOS MED. (2010), available at <http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000359> (last visited Aug. 11, 2013).

55. See discussion *infra* Part I.B.

56. 21 U.S.C. § 352 (2012).

57. *Id.*

58. See, e.g., Barbara Mintzes, PhD, et al., *Pharmaceutical Sales Representatives and Patient Safety: A Comparative Prospective Study of Information Quality in Canada, France, and the United States*, 28 J. GEN. INTERN. MED. 1395, 1400 (2013) (noting that in all three countries studied, pharmaceutical representatives rarely informed physicians about serious adverse events and observing a “serious lack of information” in pharmaceutical representative discussions about medications).

59. In addition, recent False Claims Act settlements between the Department of Justice and pharmaceutical companies show examples of these behaviors. See, e.g., United States' Notice of Intervention for Purposes of Settlement, United States *ex rel.* Wetta v. AstraZeneca Corp., C.A. No. 04-3479 (Apr. 23, 2010) (including allegations that AstraZeneca “promoted the sale and use of Seroquel to psychiatrists, other physicians (including primary care physicians) and other health care professionals in pediatric and primary care physician offices, in long-term care facilities and hospitals and in prisons for certain uses that were not approved by the Food and Drug Administration (including aggression, Alzheimer's disease, anger management, anxiety, attention deficit hyperactivity disorder, bipolar maintenance, dementia, depression, mood disorder, post-traumatic stress disorder,

The example of Vioxx illustrates every one of these techniques. Vioxx was an anti-inflammatory medication manufactured by Merck that had the side effect of increasing the risk of cardiac events.<sup>60</sup> The risk became well known within Merck early on, but as the drug became a blockbuster, Merck applied intense pressure to pharmaceutical representatives to downplay the risks and sell as much Vioxx as possible.<sup>61</sup>

On May 5, 2005, the House of Representatives' Committee on Government Reform held hearings into the marketing of Vioxx.<sup>62</sup> These hearings yielded 20,000 pages of documents describing specific actions that pharmaceutical representatives took in marketing the product.<sup>63</sup> Pharmaceutical representatives were trained in aggressive sales techniques in order to distract physicians from the heart risks associated with Vioxx.<sup>64</sup> Representatives presented only positive information about Vioxx, while downplaying or avoiding the negative information completely. Training materials showed that pharmaceutical reps were taught literally to "dodge" safety questions about Vioxx.<sup>65</sup>

The Vioxx case is hardly an anomaly—recent FDA untitled letters, warning letters, comments by physicians, and accounts written by former pharmaceutical representatives indicate that pharmaceutical representatives all too frequently overstate safety and understate warnings, in violation of federal law<sup>66</sup>:

- Representatives from Forest Laboratories, Inc., broadened the indications and minimized risks of its Daliresp (roflumilast) tablets.<sup>67</sup> Daliresp had been approved to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.<sup>68</sup> During sales calls, representatives either failed to mention the serious side effects (risk of weight loss and psychiatric events including suicidality) or responded to direct questions about these side effects with anecdotal evidence stating that other physicians were pleased with the

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and sleeplessness) . . . recruited doctors to serve as authors of articles largely prepared by medical literature companies about studies they did not conduct on unapproved uses of Seroquel; and, used those studies and articles as the basis for promotional messages about unapproved uses of Seroquel; . . . offered and paid illegal remuneration to doctors"); United States' Complaint in Intervention, United States *ex rel.* Starr v. Janssen Pharm. Prod., No. 04-cv-1529 (Nov. 4, 2013) [collectively hereinafter Settlement Documents] (alleging that Janssen marketed Risperdal as resulting in no increased risk of diabetes and that other anti-psychotics did, at the same time that Janssen was asked to add a diabetes warning to its label).

60. Merck, *supra* note 28.

61. *Id.*

62. *Id.*

63. *Id.* The full transcript is available at <http://www.gpo.gov/fdsys/pkg/CHRG-109hrg21483/html/CHRG-109hrg21483.htm>. According to documents released in the hearings, Merck representatives were instructed to use subtle gestures subconsciously to gain the trust of physicians. They were permitted to discuss only approved journal articles, defined by Merck as articles that "provide solid evidence as to why doctors should prescribe Merck products" and health risks reviewed as "obstacles" that the sales force was instructed to surmount.

64. *Id.*

65. *Id.*

66. *Id.*

67. Letter from FDA to Forest Laboratories, Inc. regarding Dalirest (roflumilast) tablets (Aug. 12, 2012), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM314572.pdf>.

68. *Id.*

drug and reported no adverse events at all.<sup>69</sup> Significantly, these actions took place despite *three such letters* from the FDA within the previous eighteen months, and the fact that Forest was operating under a Corporate Integrity Agreement that required Forest to conduct promotional activities appropriately.<sup>70</sup>

- In documents released as part of GlaxoSmithKline's \$3 billion fraud settlement, GSK employees described how they promoted medications such as Paxil and Wellbutrin for unapproved uses and downplayed safety risks.<sup>71</sup>
- Lawsuits over marketing of anti-psychotic drugs to children show that marketing efforts can obscure risks and suggest that higher-priced medications are indicated when they are not.<sup>72</sup>
- Pharmaceutical representatives undercut the package insert's warnings. Eli Lilly's sales representatives, for example, denied that weight gain was a problem in connection with Zyprexa, even though that side effect was listed on the package insert.<sup>73</sup> "They were trying to press hard," one physician told the *Wall Street Journal*, "[t]hey would not acknowledge it was a concern."<sup>74</sup>
- Pharmaceutical representatives targeted District of Columbia Medicaid recipients in their marketing of anti-psychotic drugs, to the point that "it is likely that much of the antipsychotic prescribing to D.C. Medicaid beneficiaries may be inappropriate."<sup>75</sup> A report by the government of the District of Columbia on pharmaceutical marketing and prescription of anti-psychotic drugs to children found that "[a]ntipsychotic manufacturers are marketing heavily to District psychiatrists, and appear to be targeting

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69. *Id.*

70. *Id.*

71. Ben Adams, *Another Failing, But Will Industry Learn?*, PHARMAFILE (Apr. 7, 2012), [www.pharmafile.com/news/173307/gsk-ruling-another-failing-will-industry-learn](http://www.pharmafile.com/news/173307/gsk-ruling-another-failing-will-industry-learn) (explaining how pharmaceutical representatives discussed the use of Paxil in children and downplayed risks, even though GSK had data stating that the use of Paxil in people under the age of eighteen was not only ineffective but increased the risk of suicide).

72. See Settlement Documents, *supra* note 59. Every major seller of anti-psychotic drugs has been either under government investigation or has settled lawsuits brought by the government. Duff Wilson, *Side Effects May Include Lawsuits*, N.Y. TIMES, Oct. 2, 2010 ("Lawyers suing AstraZeneca say documents they have unearthed show that the company tried to hide the risks of diabetes and weight gain associated with the new drugs. Positive studies were hyped, the documents show; negative ones were filed away.").

73. Rockoff, *supra* note 5 (noting that several physicians told the Wall Street Journal about instances in which sales representatives downplayed or denied warnings). The article notes, however, that in response to federal scrutiny and physicians' impatience with the traditional hard sell pharmaceutical representatives are also softening their marketing approach towards physicians. *Id.*

74. *Id.*

75. Liz Borkowski et al., *Impacts of Pharmaceutical Marketing on Healthcare Services in the District of Columbia*, DEPARTMENT OF HEALTH (July 31, 2012), <http://doh.dc.gov/sites/default/files/dc/sites/doh/publication/attachments/Impacts%20of%20Pharmaceutical%20Marketing%20on%20Healthcare%20Services%20in%20the%20District%20of%20Columbia%20-%20with%20logo.pdf>.

Medicaid psychiatrists in particular.<sup>76</sup> Medicaid psychiatrists received 66 percent of all pharmaceutical gifts and payments to psychiatrists, although they represented only 26 percent of the psychiatrists.<sup>77</sup> One in ten D.C. Medicaid recipients received an anti-psychotic prescription, a rate five times higher than the national population.<sup>78</sup>

- In a single brochure that Shire gave to kidney patients about Fosrenol, the FDA said the company committed four separate violations: It left out the risk warnings, which include Crohn’s disease and bowel obstruction.<sup>79</sup> It said Fosrenol was safer and more effective than other drugs, while the FDA saw no evidence to support comparative claims like that.<sup>80</sup> It said Fosrenol could prevent “bone disease, heart disease or death,” when there was no evidence supporting that conclusion.<sup>81</sup>
- In one case of literally hiding the risks, Shire Pharmaceuticals was warned that a promotional magnet it was distributing did not comply with regulations regarding promotional materials.<sup>82</sup> The magnet included the advantages and risks associated with Vyvanse, a medication designed to treat Attention Deficit Hyperactivity Disorder (ADHD) in children.<sup>83</sup> The magnet also functioned as a business card holder—but when a card was inserted, the card obscured all the warnings, leaving only the advantages visible.<sup>84</sup> The FDA sent a warning letter to Shire, asking that it discontinue use of the magnet.<sup>85</sup>
- Even CEOs have drawn warning letters for failing to mention serious risks while promoting drugs. The CEO of Aegerion Pharmaceuticals appeared twice on the CNBC show “Fast Money,” promoting the company’s Juxtapid drug, and making “substantial and repeated claims of efficacy . . . without **any** of the risks associated with these new intended uses.”<sup>86</sup>

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76. *Id.* at 36-42.

77. *Id.*

78. *Id.* at 34.

79. Warning Letter from FDA to Shire Pharmaceuticals (Nov. 5, 2009), *available at* <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM190451.pdf> (noting “repeated” violations).

80. *Id.*

81. *Id.*

82. Warning Letter from FDA to Shire Pharmaceuticals (June 20, 2011), *available at* <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm259167.htm>.

83. *Id.*

84. *Id.*

85. *Id.*

86. 21 C.F.R. 201.56 (2013); Letter from FDA to Aegerion Pharmaceuticals, Inc. (Nov. 8, 2013), *available at* <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/enforcementactivities-byfda/warninglettersandnoticeofviolationletterstopharmaceuticalcompanies/ucm374338.pdf>.

II. A HOST OF REGULATIONS AND NEW ETHICS INITIATIVES DO NOT DECREASE  
AGGRESSIVE MARKETING AND ANTI-WARNINGS

Pharmaceutical manufacturers are subject to federal regulations and the FDA's authority to enforce them. Yet pharmaceutical representatives are still able to present one-sided information about their products by appealing to physicians directly and in person, in the context of cozy relationships. The FDA's enforcement mechanisms—characterized by repeated warnings and opportunities to comply—have come to be regarded as slaps on the hand that are part of doing business.

A. *Extensive Regulations Apply to Pharmaceutical Labeling and Promotional Materials*

The FDA is responsible for approving pharmaceutical labeling and for regulating pharmaceutical marketing.<sup>87</sup> Several significant federal statutes and a number of regulations apply to pharmaceutical sales and marketing.<sup>88</sup>

Modern federal regulation of pharmaceuticals began with the 1906 Pure Food and Drugs Act.<sup>89</sup> The regulations later developed further, largely in response to a series of public health crises caused by unsafe medications.<sup>90</sup> In 1937, a new pediatric sulfanilamide drug killed over one hundred people, many of them children. The public reaction resulted in a legislative safety mandate for drugs, as well as a prohibition on false therapeutic claims.<sup>91</sup> The resulting Federal Food, Drug, and Cosmetic Act of 1938 ("FDCA") requires that safety of new drugs be tested and that the FDA be notified before the new drug is brought to market.<sup>92</sup>

Another public health tragedy brought further regulation, this time caused by the morning sickness drug, thalidomide.<sup>93</sup> Thalidomide caused stillbirths and limb malformations in babies.<sup>94</sup> Reacting to this disaster, Congress in 1962 changed the way the FDA regulated new drugs so as to require "premarket approval of the safety and effectiveness

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87. John P. Swann, *FDA's Origin*, FDA (Jan. 23, 2014), <http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm124403.htm> (noting that "[s]tates exercised the principal control over domestically produced and distributed foods and drugs in the 19th century, control that was markedly inconsistent from state to state"). Regulation of pharmaceuticals began in the United States as a matter handled on an inconsistent, state-by-state basis. *Id.* Today, regulation of pharmaceuticals takes place principally at the federal level, through the FDA. *Id.*

88. The Controlled Substances Act, the Poison Prevention Packaging Act, the Omnibus Budget Reconciliation Act of 1990), and the Health Insurance Portability and Accountability Act (HIPAA) together with associated regulations, are part of the federal government's regulation of pharmaceuticals and pharmacies. See THOMAS R. FULDAN & ALBERT I. WERTHEIMER, PH.D, HANDBOOK OF PHARMACEUTICAL PUBLIC POLICY (Haworth Press 2007); The False Claims Act, 31 U.S.C. § 3729(a)(1)(A) & (B); the Federal Anti-Kickback Statute, 42 U.S.C. § 1320a-7b; Stark, and the FDCA also apply.

89. Pub. L. No. 59-384, 34 Stat. 768 (1906) (*repealed by* Food, Drug and Cosmetic Act (1938), Pub. L. No. 75-717, 1938, 52 Stat. 1059).

90. Swann, *supra* note 87.

91. *Id.*

92. Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-300 (2000)).

93. *The Independent Institute, History of Federal Regulation: 1902-Present*, FDAREVIEW.ORG, available at <http://www.fhareview.org/history.shtml> (last visited Aug. 11, 2013).

94. *Id.* (stating that thalidomide was a treatment for morning sickness that led to stillbirths and birth defects, particularly limb malformations).

of every new drug.”<sup>95</sup> Approval of a new pharmaceutical now requires clinical trials<sup>96</sup> and a New Drug Application.<sup>97</sup> The NDA permits FDA to balance the safety and efficacy of the new drug, to assess the risks, and to determine appropriate warnings.<sup>98</sup> To fund the application process, pharmaceutical companies pay a fee.<sup>99</sup>

Federal regulations emphasize the need for thorough and complete warnings accompanying each pharmaceutical. The regulations call for proper “labeling,” which, by definition, includes all labels and any written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.<sup>100</sup> The labeling must portray the drug’s safety profile with “accuracy, balance, and brevity.”<sup>101</sup> In doing so, the manufacturer must include a full description of the drug, as well as safety information concerning indications and usage, dosage, and administration.<sup>102</sup>

With regard to warning information, the labeling must contain the “boxed warnings” and other cautionary language, such as “[r]ecent major changes,” which includes newly authorized language, and “[c]ontraindications,” which includes situations or conditions under which the pharmaceutical in question should not be prescribed.<sup>103</sup> The labeling contains a separate section specifically for “warnings and precautions.”<sup>104</sup> This section should include the most significant information that would affect a prescriber’s decision to select this particular pharmaceutical for a particular patient.<sup>105</sup> All “material” information must be included.<sup>106</sup>

A drug’s labeling is often controversial and dynamic rather than static. That is, when

95. See Kefauver-Harris Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (codified at 21 U.S.C. §§ 321-399 (2000)).

96. The manufacturer must present “substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling,” 21 U.S.C. § 355(d)(5). The NDA shall include: (1) reports of the clinical trials and testing done to determine the safety and effectiveness of the drug; (2) the complete ingredients or components of the drug; (3) the composition of the drug; (4) a complete description of the manufacturing, processing, and packaging methods and controls; (5) samples of the drug and its components (if requested); and (6) samples of the proposed labeling, 21 U.S.C. § 355(b)(1) (2012).

97. To obtain approval for a new drug, the manufacturer must first submit an investigational new-drug application (“IND”) to the FDA. The IND must include information about the drug’s chemistry, manufacturing, pharmacology, and toxicology, see 21 U.S.C. § 355(b); 21 C.F.R. § 312.21. The IND must also include information about the animal pharmacology and toxicology of the drug, and details regarding the protocols for human testing.

98. Victor E. Schwartz, Phil Goldberg, *A Prescription for Drug Liability and Regulation*, 58 OKLA. L. REV. 135, 141 (2005) (citing Victor E. Schwartz, *Unavoidably Unsafe Products: Clarifying the Meaning and Policy Behind Comment k*, 42 WASH. & LEE L. REV. 1139, 1142 (1985) (noting that “[a] principal focus of the Food and Drug Administration, apart from safety, is efficacy. Since every drug includes some risks, the Food and Drug Administration regards efficacy as essential—if one is to take risks, he or she should obtain the desired result.”)).

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

100. 21 U.S.C. 321(m) (2012).

101. 21 C.F.R. pt. 201 (2005) (setting out the requirements for pharmaceutical labeling, such as substantive requirements and requirements that warnings be suitably prominent and in certain fonts).

102. *Id.* § 201.57(a).

103. *Id.* § 201.57(a)(9).

104. *Id.* § 201.57(a)(10). This section should include “[a] concise summary of the most clinically significant information required under paragraph (c)(6)[.]” *Id.*

105. *Id.*

106. 21 C.F.R. 1.21 (2005) (“(a) Labeling of a food, drug, device, cosmetic, or tobacco product shall be deemed to be misleading if it fails to reveal facts that are: (1) Material in light of other representations made or suggested by statement, word, design, device or any combination thereof; or (2) Material with respect to consequences which may result from use of the article under: (i) The conditions prescribed in such labeling or (ii) such conditions of use as are customary or usual.”).



the label is first created, it may be the subject of intense negotiation between the pharmaceutical manufacturer and the FDA. In addition, the label may be amended over the life of the drug, as people use the drug in greater numbers and for a longer period of time than in clinical trials.<sup>107</sup> This broader use often results in the discovery of additional safety information that must be added to the label.<sup>108</sup> These amendments too are often hotly contested, taking months to enact.<sup>109</sup> The FDA may, for example, request that the manufacturer include certain specific information, but the manufacturer may argue against the inclusion of the requested information, or ask that other information be included. The result is usually a negotiated version in which the parties arrive at a final version acceptable to both sides.<sup>110</sup>

In terms of written warnings, particularly the package insert that must be preapproved by the FDA, the language is carefully chosen and vetted. As discussed below, however, the emphasis on the package insert is no more than paper compliance when pharmaceutical representatives can undermine and deny these carefully crafted warnings.

### B. *Promotion and Advertising are Regulated*

Like drug labeling, drug promotion is regulated by the FDA.<sup>111</sup> Promotion, including pharmaceutical representatives' interactions with physicians, is regulated by laws, policies, and ethical guidelines at the federal and state levels. Federal regulations and guidance governing pharmaceutical representatives are issued by the FDA and Office of the Inspector General (OIG).<sup>112</sup>

Promotional labeling is information given to consumers or prescribers directly, while advertising is usually broadcast on television or radio, or published in newspapers or magazines.<sup>113</sup> Among the regulations are those addressing the "brief summary" and "true statement" requirements.<sup>114</sup> A statement fails to be a "true statement" if it is false or misleading with respect to side effects, contraindications, or effectiveness, if it fails to provide a "fair balance" of information on these subjects, or if it does not provide material

107. See, e.g., David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims*, 96 GEO. L.J. 461, 466 (2008).

108. *Id.*

109. *Id.* at 480 ("[T]he FDA acknowledges that it took over a year to force Merck, the manufacturer of Vioxx, to add a warning of the risks of heart attack and stroke to Vioxx's label. During the lengthy negotiations, no change was made to Vioxx's label, and in the end, the FDA settled for a weaker warning than it had proposed.")

110. *Id.*

111. The FDA is responsible for "preventing misbranding of . . . drugs . . . shipped in interstate commerce," as well as the "regulation of truth or falsity of prescription drug advertising." FDA, *Memorandum of Understanding Between the Federal Trade Commission and the Food and Drug Administration*, MOU 225-71-8003 (1971), available at <http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstanding-MOUs/DomesticMOUs/ucm115791.htm> (last updated Mar. 10, 2009).

112. 21 C.F.R. 200-203 (2013). See, e.g., *Guidance for Industry: Industry-Supported Scientific and Educational Activities*, HHS-FDA (Nov. 1997), <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM125602.pdf>; *OIG Compliance Program Guidance Program Guidance for Pharmaceutical Manufacturers*, HHS-OIG (Apr. 18, 2003), <https://oig.hhs.gov/authorities/docs/03/050503FRCPGPharmac.pdf>.

113. The FDCA does not define "advertising," but the regulations list items that are regulated as advertisements, such as "advertisements in published journals, magazines, other periodicals, and newspapers, and advertisements broadcast through media such as radio, television, and telephone communications systems." 21 C.F.R. § 202.1(1)(1) (2013); *Drug Advertising: A Glossary of Terms*, FDA, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072025.htm> (last visited Aug. 12, 2013).

114. 21 C.F.R. 202.1(e)(3)-(7).

facts about the drug's use or representations made in the advertisement.<sup>115</sup>

The FDA monitors advertising and takes action when companies violate the regulations.<sup>116</sup> To enforce its regulations, a division of the FDA known as the Office of Prescription Drug Promotion (OPDP) monitors prescription drug promotion for compliance with the law, and reviews Form FDA-2253 submissions. OPDP representatives attend conferences and collect promotional materials for review, send warning letters, and take other enforcement actions, such as recalls, seizures, injunctions, administrative detentions, and criminal prosecutions.<sup>117</sup> The states also regulate pharmaceutical representatives; some of these regulations are stricter than those at the federal level.<sup>118</sup>

C. *Self-Policing and Ethics Policies have made some Inroads but Remain Incomplete*

Recognizing that pharmaceutical marketing can present conflicts of interest, some major academic medical centers, industry organizations, and health insurance companies have developed their own ethics rules or guidelines addressing contact between pharmaceutical representatives and healthcare providers. While these rules and guidelines represent positive progress, they are either non-binding or do not reach far enough to disrupt the relationship between the pharmaceutical industry and healthcare providers. In 2002, the pharmaceutical industry organization, PhRMA, adopted its Code on Interactions with Healthcare Professionals, which was revised in 2008.<sup>119</sup> Many of the signatories, however, also appear on the Office of the Inspector General's list of companies with corporate integrity agreements or negotiated settlements with the OIG.<sup>120</sup> The fact that the corporate integrity agreements mainly post-date the 2008 Code indicates that the Code has not solved the problem of physician-representative interactions.<sup>121</sup> National organizations have also

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115. Bruce N. Kuhlik, *The FDA's Regulation of Pharmaceutical Communications in the Context of Managed Care: A Suggested Approach*, 50 FOOD & DRUG L.J. 23, 38 (1995) (“[f]air balance” means that the materials contain “overall, a balanced presentation of the risks and benefits that can affect a health care practitioner’s decision to prescribe the promoted product.”).

116. One exception to the usual lack of preapproval is when the advertising concerns a drug that can be fatal, and the risk of fatality has not been widely publicized in the medical literature. 21 C.F.R. §202.1(j)(1).

117. KATHLEEN M. BOOZANG & SIMONE HANDLER-HUTCHINSON, PHARMACEUTICAL & MEDICAL DEVICE COMPLIANCE MANUAL 192 (2012). As one example, the FDA issued a warning letter where a mailer for Cymbalta did not include the necessary warnings and overstated effectiveness. The mailer also indicated that the recipient would be receiving a leather desk letter holder. Letter from FDA to Eli Lilly and Company (Jan. 7, 2010), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm054170.pdf>.

118. Safe Rx Amendment Act of 2008, D.C. CODE § 48-844 (2008) (stating that the District of Columbia requires pharmaceutical representatives to be licensed to sell pharmaceuticals).

119. *Code on Interactions with Healthcare Professionals*, PHRMA, available at <http://phrma.org/sites/default/files/pdf/SignatoryCompaniesCodeonInteractionswithHealthcareProfessionals.pdf> (last visited Nov. 22, 2013) (the code “reaffirms that interactions between pharmaceutical company representatives and healthcare professionals should be focused on informing the healthcare professionals about products, providing scientific and educational information, and supporting medical research and education”).

120. *List of Companies with Corporate Integrity Agreements*, OIG, available at <http://oig.hhs.gov/compliance/corporate-integrity-agreements/cia-documents.asp> (last visited Nov. 22, 2013).

121. *Id.*

issued guidelines for pharmaceutical representative-physician interactions, although compliance with these is—with certain exceptions<sup>122</sup>—voluntary.<sup>123</sup> Indeed, one consultant describes the guidelines as a prophylactic attempt against further external regulation: “[The set of guidelines] is an attempt to self-police and thereby ward off further external restrictions.”<sup>124</sup>

In addition, individual hospitals, academic medical centers, or practices may also have guidelines addressing interactions between pharmaceutical sales representatives and physicians. These range from requirements that visitors register in advance to strict rules for pharmaceutical representatives’ behavior, and access to physicians. These regulations—together with other factors such as physicians’ increasingly busy schedules—have resulted in an increase in physicians’ refusing to see pharmaceutical representatives.<sup>125</sup> Pharmaceutical representatives continue to press for access, however, and are urged to consider alternative avenues of contact, such as on-demand media and other points of contact.<sup>126</sup>

When others question the value of pharmaceutical industry/physician interactions, physicians often cite an educational value of these contacts.<sup>127</sup> The vast number of studies and trials that are published on a daily basis are all but overwhelming for a busy physician seeking to stay abreast of the newest information. But industry detailing is not the only approach to disseminating information about new drugs. Another recently-developed approach called “academic detailing” aims to disseminate information gleaned from medical literature and assessed in a “non-product-given” way.<sup>128</sup> In this fashion, a non-profit organization such as the Independent Drug Information Service disseminates information to physicians.<sup>129</sup>

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122. A handful of states have incorporated the PhRMA code as part of their state laws. For example, Nevada requires that pharmaceutical companies adopt the PhRMA code or another code that would

[Establish] the practices and standards that govern the marketing and sale of its products.

The marketing code of conduct must be based on applicable legal standards and incorporate principles of health care, including, without limitation, requirements that the activities of the wholesaler or manufacturer be intended to benefit patients, enhance the practice of medicine and not interfere with the independent judgment of health care professionals.

NEV. REV. STAT. § 639.570 (2007).

123. The Accreditation Council for Continuing Medical Education (ACCME) has issued restrictions on the extent to which pharmaceutical sales representatives can participate in medical education. *Standards for Commercial Support*, ACCME, [www.accme.org/requirements/accreditation-requirements-cme-providers/standards-for-commercial-support](http://www.accme.org/requirements/accreditation-requirements-cme-providers/standards-for-commercial-support) (last visited December 28, 2012).

124. Wendy Heckelman, *The Changing Pharmaceutical Sales Landscape* (Oct. 7, 2009), available at <http://www.pharmexec.com/pharmexec/Sales/The-Changing-Pharmaceutical-Sales-Landscape/ArticleStandard/Article/detail/632252?contextCategoryId=47505>.

125. *Drug Makers Try Cures for Physician “Cold Shoulders”*, ZS ASSOCIATES, <http://www.zsassociates.com/about/news-and-events/drug-makers-try-cures.aspx> (last visited Dec. 28, 2012).

126. *Id.*

127. *Physician Payment Sunshine Act: Physicians and life sciences coming to terms with transparency?*, DELOITTE (2012), [https://www.deloitte.com/assets/Dcom-Global/Local%20Assets/Documents/LSHC/dttl\\_lshc\\_ForbesInsightsLSHCTransparencyReport.pdf](https://www.deloitte.com/assets/Dcom-Global/Local%20Assets/Documents/LSHC/dttl_lshc_ForbesInsightsLSHCTransparencyReport.pdf) (noting that physicians believe industry-sponsored continuing medical education is useful for learning about new medications); Johar, *supra* note 8, at 330 (“Interactions between physicians and representatives can be positive, informative, balanced, and provide information that will help patients”).

128. Jerry Avorn, *Healing the Overwhelmed Physician*, N.Y. TIMES, June 11, 2013, at A27 (noting that “even the most superbly assemble evidence doesn’t disseminate itself”).

129. The Independent Drug Information Service is funded by the governments of Pennsylvania and the District of Columbia. *Independent Drug Information Source (IDIS)*, ALOSA, <http://www.alosafoundation.org/independent-drug-information-service/> (last visited Aug. 23, 2014). Other health systems such as that of Australia and

D. *FDA's Collaborative Approach to Enforcement Leaves Gaps for Non-Compliance*

Compliance with these regulations and guidelines has been uneven. The FDA has broad powers to enforce its regulations through a variety of means, including untitled letters, warning letters, fines, and consent decrees,<sup>130</sup> as well as seizure of misbranded pharmaceuticals.<sup>131</sup> The Office of the Inspector General of the U.S. Department of Health and Human Services can also enforce misconduct where Health and Human Services programs such as Medicare and Medicaid are involved.<sup>132</sup>

Two factors combine, however, to make enforcement difficult: first, the sheer scale of the promotional effort makes enforcement challenging—there are 81,000 pharmaceutical representatives in the United States<sup>133</sup> and countless conferences and presentations in which marketing takes place. Second, when pharmaceutical marketing efforts do violate the rules, the FDA's first step in compliance is generally to ask the company to cease the offensive actions.<sup>134</sup> That is, before taking more drastic actions, the FDA often issues an untitled letter or warning letter setting out the violation and asking the company to stop taking the offending action.<sup>135</sup> The offending company is then expected to stop taking the offensive action, but no other penalty is applied—compliance is voluntary.<sup>136</sup> Significantly, though, the FDA is not in physicians' offices and cannot monitor the thousands of in-person encounters between physicians and representatives.<sup>137</sup>

Officials at the FDA have observed that companies take a calculated approach to warning letters, simply accepting warning letters as part of doing business and doing little or nothing in response.<sup>138</sup> This corporate approach, while undesirable from a safety perspective, is perhaps logical, considering that even repeated failures to comply with the

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Kaiser Permanente, have adopted this approach to disseminating information about new drugs. *Id.* After all, if pharmaceutical marketing results in the prescription of more and more expensive medications, counter-acting such marketing would result in very significant cost savings. Funding of such a system might well prove worth an investment by insurers and governments paying for these medications.

130. BOOZANG & HANDLER-HUTCHINSON, *supra*, note 118, at 8.

131. 21 U.S.C. § 334(a) (2012).

132. BOOZANG & HANDLER-HUTCHINSON, *supra* note 118, at 301.

133. Debra Gordon, *Dealing with Drug Reps*, PHYSICIANS PRACTICE, <http://www.physicianspractice.com/articles/dealing-drug-reps> (last visited July 20, 2013).

134. MICHAEL E. CLARK, PHARMACEUTICAL LAW: REGULATION OF RESEARCH, DEVELOPMENT, AND MARKETING 22 (2007).

135. *See FDA Initiates Seizure of Potentially Dangerous Drugs from Repackager*, FDA NEWS (Sept. 15, 2003), available at <http://www.fda.gov/bbs/topics/NEWS/2003/NEW00945.html>. Warning letters are available at <http://www.accessdata.fda.gov/scripts/wlcfm/sindex.cfm>.

136. "Warning letters are issued to achieve voluntary compliance and to establish prior notice . . . Warning letters are issued only for violations of regulatory significance. Significant violations . . . may lead to enforcement action if not promptly and adequately corrected. A Warning Letter is the agency's principal means of achieving prompt voluntary compliance with the . . . [FDCA]." FDA Regulatory Procedures Manual §4-1-1 ("Warning Letter Procedures") (2011), available at [http://www.fda.gov/ora/compliance\\_ref/rpm/](http://www.fda.gov/ora/compliance_ref/rpm/); CLARK, *supra* note 134, at 227 (noting that "[t]he FDA ordinarily uses a stair-step approach to enforce the FDCA, first trying to get members of the regulated community to voluntarily comply with the requirements of the FDCA and its implementing regulations before using stricter measures.").

137. Kate Greenwood, *The Ban on "Off-Label" Pharmaceutical Promotion: Constitutionally Permissible Prophylaxis Against False or Misleading Commercial Speech?*, 37 AM. J.L. & MED. 278, 296 (2011) (noting pharmaceutical companies' difficulties in self-monitoring under these circumstances).

138. *Schering-Plough GMP Consent Decree Puts Drug Industry on Notice*, The Food & Drug Letter 1, June 7, 2002, available at <http://brucegoldfarb.com/FDL1.pdf> (noting that "[t]he agency has allowed itself to get into this situation of issuing warning letter after warning letter to the same company, without taking any action," said Eric Blumberg, the FDA's deputy chief counsel for litigation, who signed the decree. "The FDA has tried to send

regulations often draw no penalty other than a request to “cease violative promotional activities.”<sup>139</sup>

In the case of Vioxx, for example, the downplaying of risks took place long after Merck received a warning letter on September 17, 2001 asking it to cease its downplaying of warnings.<sup>140</sup> And even when companies are under negotiated agreements known as “corporate integrity agreements,” in which companies agree to strengthen their compliance program, overly-aggressive marketing and downplaying of warnings may still continue. A recently filed case against Novartis suggests that its corporate integrity agreement did little to curtail a speaker program that was allegedly no more than a vehicle to give prescribers money and lavish meals.<sup>141</sup>

Likewise, a corporate integrity agreement did not dissuade Forest Laboratories, Inc., from overstating benefits, downplaying risks, and broadening the indications of its Daliresp (roflumilast) tablets.<sup>142</sup> Significantly, these actions took place despite three previous such letters from the FDA within the previous eighteen months, and the fact that Forest was operating under a Corporate Integrity Agreement that specifically mentioned the need to conduct promotional activities appropriately.<sup>143</sup> Hospira also received multiple warning letters that seemed to have no impact on its activities.<sup>144</sup>

In one recent effort, the FDA has asked physicians to inform the FDA if pharmaceutical representatives downplay risks.<sup>145</sup> Reporting physicians can remain anonymous if

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the message out that that’s not going to happen anymore.”).

139. Letter from FDA, *supra*, note 68 (where, for example, Forest Laboratories, Inc., allegedly violated its Corporate Integrity Agreement by broadening the indications and minimized risks of the drug Daliresp (roflumilast) tablets, it was asked simply to “cease” these activities, despite the fact that it had received three such letters from the FDA within the previous eighteen months).

140. Warning Letter from FDA to Merck (Sept. 17, 2001), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersand-NoticeofViolationLetterstoPharmaceuticalCompanies/UCM166383.pdf>; Letter from Representative Harry Waxman to the Democratic Members of the Government Reform Committee at 28-29 (May 5, 2005), available at <http://oversight-archive.waxman.house.gov/documents/20050505114932-41272.pdf> (citing MERCK, CHAMPION SELLING: MILESTONE LEADER’S GUIDE (Jan. 2002)).

141. The government alleges as follows:

[E]ven after entering into the corporate integrity agreement, Novartis’s compliance program failed to prevent kickbacks from being paid in conjunction with Novartis’s speaker programs. No individual at the company was tasked with examining its speaker program data to determine whether the programs were used for an illegitimate purpose. Furthermore, although instances of speaker program abuse were reported to Novartis, sanctions were generally mere slaps on the wrist. In some cases, sales representatives who violated Novartis’s own speaker program policies were nevertheless promoted. Even after September 2010, Novartis continued to conduct bogus speaker programs that were simply vehicles for paying kickbacks to doctors in the form of honoraria and expensive meals.

Ed Silverman, *Did Novartis Violate Its Corporate Integrity Agreement?*, FORBES (Apr. 27, 2013), available at <http://www.forbes.com/sites/edsilverman/2013/04/27/did-novartis-violate-its-corporate-integrity-agreement/>.

142. Letter from FDA, *supra*, note 68.

143. *Id.*

144. Ed Silverman, *Another Day, Another Warning Letter for Hospira but Will FDA Issue a Consent Decree?* FORBES (May, 31, 2013), available at <http://www.forbes.com/sites/edsilverman/2013/05/31/another-day-another-warning-letter-for-hospira-but-will-the-fda-issue-a-consent-decree/>.

145. The FDA’s website describes the Bad Ad program as follows:

FDA’s Bad Ad program is an outreach program designed to educate healthcare providers about the role they can play in helping the agency make sure that prescription drug advertising and promotion is truthful and not misleading. The Bad Ad Program is administered by the agency’s Office of Prescription Drug Promotion (OPDP) in the Center for Drug Evaluation and Research. The program’s goal is to help raise awareness among healthcare

they prefer to do so.<sup>146</sup> While physicians, as the recipients of the potentially bad information, certainly have access to the improper information, this manner of enforcement is problematic at best, given that pharmaceutical representatives work hard to create a relationship with physicians. And, according to one survey, however, only three out of ten health care providers were aware of the program, and some physicians indicated that it is unrealistic to expect them to act as enforcers of the FDA's rules.<sup>147</sup>

Thus, despite the extensive number of regulations and efforts to enforce them, over-promotion of pharmaceuticals and understatement of warnings continue to take place.

### III. COURTS SHOULD CONSIDER BOTH WARNINGS AND ANTI-WARNINGS

Those who are harmed by a pharmaceutical company's failure-to-warn can sue in state court under theories of tort liability. In a failure-to-warn case, plaintiffs allege insufficiency of the warnings concerning a pharmaceutical's side effects or use. Failure-to-warn cases are difficult to win, however, because courts tend to focus on the package insert as the "reasonable" warning, rather than pharmaceutical representatives' statements about the dangers. As set out below, this narrow focus on the package insert is problematic because it ignores the actual flow of information to physicians regarding the safety and appropriateness of a particular medication. Instead of narrowly focusing on the package insert, courts should take *all* the warning and anti-warning information, including safety-related marketing information, into account when deciding the reasonableness of a warning.

#### A. Failure-To-Warn Liability Turns on the Presence of a "Reasonable" Warning

Generally, a person who supplies a dangerous product directly or through another person or entity is liable for damage caused by the product.<sup>148</sup> Comment b to Section 6 of the Third Restatement of Torts crafts a basis for prescription drug-related liability, taking into account that prescription drugs are inherently dangerous and cannot be made completely safe, even when used for their intended purpose.<sup>149</sup>

A pharmaceutical manufacturer can be held liable for failure to warn if the manufacturer does not provide an accurate picture of the dangers associated with the product.

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providers about misleading prescription drug promotion and provide them with an easy way to report this activity to the agency: e-mail [BadAd@fda.gov](mailto:BadAd@fda.gov) or call 855-RX-BADAD.

*Truthful Prescription Drug Advertising and Promotion*, FDA, <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/DrugMarketingAdvertisingandCommunications/ucm209384.htm> (last visited Feb. 22, 2013).

146. *Id.*

147. *How Are Physicians Responding to FDA's Bad Ad Program?*, PR WEB (Mar. 4, 2011), available at <http://www.prweb.com/releases/doctordirectory/badad/prweb8105854.htm> (noting survey results in which some physicians stated unwillingness to inform on pharmaceutical representatives, while others said they would do so if necessary; others noted the lack of time in physicians' schedules and physicians' concerns with following regulations themselves rather than worrying about enforcing regulations regarding others' behavior).

148. *Stevens v. Parke, Davis & Co.*, 507 P.2d 653 (Cal. 1973) (citing RESTATEMENT (SECOND) OF TORTS § 388 (1965); A person who supplies a dangerous product directly or through another person or entity is liable for damaged caused by the product, if the product is used as intended by those expected to use it and the supplier "(a) knows or has reason to know that the [product] is or is likely to be dangerous for the use for which it is supplied, and (b) has no reason to believe that those for whose use the [product] is supplied will realize its dangerous condition, and (c) fails to exercise reasonable care to inform them of its dangerous condition or of the facts which make it likely to be dangerous.").

149. RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 6 cmt. b (1998).

The Third Restatement of Torts explains that to be considered reasonably safe, “reasonable instructions or warnings” must be given to prescribing healthcare providers.<sup>150</sup> With regard to warnings, therefore, the test is one of reasonableness under the circumstances rather than strict liability.<sup>151</sup> The following are factors that determine whether a warning is adequate as a matter of law: (1) The warning must state the significant risks involved and be factually correct;<sup>152</sup> (2) the warning must have the physical attributes such that a reasonably prudent person would be alerted to the dangers;<sup>153</sup> (3) the warning must communicate the seriousness of the harm that may result; (4) the warning cannot be ambiguous, equivocal, or contradictory;<sup>154</sup> (5) the warning should be easily understood by the intended audience; and (6) the warning should be communicated by the most appropriate means.<sup>155</sup> The mere mention of a possible injury or side effect may not be adequate.<sup>156</sup> When the court considers the warning to consist of the package insert and nothing else, analysis of the package insert using these factors usually results in the warning being found sufficient, provided that the risk at issue was included in the insert.

Significantly, this warning need not be given to pharmaceutical manufacturers’ ultimate customers—patients.<sup>157</sup> This doctrine, known as the “learned intermediary” defense,

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150. The Restatement defines a failure-to-warn defect as follows: “A prescription drug or medical device is not reasonably safe due to inadequate instructions or warnings if reasonable instructions or warnings regarding foreseeable risks of harm are not provided to: (1) prescribing and other [healthcare] providers who are in a position to reduce the risks of harm in accordance with the instructions or warnings; or (2) the patient when the manufacturer knows or has reason to know the [healthcare] providers will not be in a position to reduce the risks of harm in accordance with the instructions or warnings,” *id.* at § 6(d).

151. *See, e.g.*, Richard C. Ausness, *Learned Intermediaries and Sophisticated Users: Encouraging the Use of Intermediaries to Transmit Product Safety Information*, 46 SYRACUSE L. REV. 1185, 1192 (1996). *See also* Brochu v. Ortho Pharm. Corp., 642 F.2d 652, 657 (1st Cir. 1981) (“An adequate warning is one reasonable under the circumstances.”); Graham v. Wyeth Lab., 666 F. Supp. 1483, 1498 (D. Kan. 1987) (“An adequate warning is one that is reasonable under the circumstances.”); Ortho Pharm. Corp. v. Chapman, 388 N.E.2d 541, 553 (Ind. Ct. App. 1979) (“To be adequate, a warning must be reasonable under the circumstances.”).

152. *See* Little v. Liquid Air Corp., 939 F.2d 1293, 1300 (5th Cir. 1991) (noting that “a manufacturer or distributor ‘fulfills its duty to warn in this context only if it warns of all dangers associated with its products of which it has actual or constructive knowledge.’”) (quoting Jackson v. Johns-Manville Sales Corp., 750 F.2d 1314, 1320 (5th Cir. 1985)); Deines v. Vermeer Mfg. Co., 755 F. Supp. 350, 353 (D. Kan. 1990) (“The manufacturer’s duty is to warn of all potential dangers which it knew, or in the exercise of reasonable care should have known, to exist.”); *In re Meridia*, 328 F. Supp. 2d 791, 812 (N.D. Ohio 2004) (citing Pittman v. Upjohn Co., 890 S.W.2d 425, 429 (Tenn. 1994)) (noting that a pharmaceutical company’s warning to physicians is considered adequate if it “contain[s] a full and complete disclosure of the potential adverse reactions to the drug.”).

153. Seley v. G.D. Searle & Co., 423 N.E.2d 831 (Ohio 1981) (“A warning is adequate . . . where, under all the circumstances, it reasonably discloses to the medical profession all risks inherent in the use of the drug which the manufacturer knew or should have known to exist.”).

154. *See, e.g.*, Givens v. Lederle, 556 F.2d 1341, 1345 (5th Cir. 1977) (a warning for an oral polio vaccine was potentially inadequate where it stated the risk of paralysis was one in three million, but then cast doubt on the causal link between the vaccine and the paralysis); Salmon v. Park, Davis & Co., 520 F.2d 1359, 1363 (4th Cir. 2012) (statement expressing doubt about causal connection between chloramphenicol and aplastic anemia diluted a disclosure stating the need to take precautions against anemia). As explained in further detail above, *supra* Section I.B, a warning may also be diluted by subsequent advertising and promotional activities which downplay the product’s risks. *See* Stevens v. Parke, Davis & Co., 507 P.2d 653, 662 (Cal. 1973) (warning provided to physicians by drug company about the risk of aplastic anemia from administration of Chloromycetin antibiotic to patients was nullified by subsequent overpromotion); Incolligo v. Ewing, 282 A.2d 206, 220 (Pa. 1971) (warning provided to physicians by drug company about the risk of aplastic anemia from administration of Chloromycetin antibiotic to patients was nullified by subsequent overpromotion).

155. *Id.*

156. *In re Meridia*, 328 F. Supp. 2d at 812 (citing Stahl v. Novartis Pharm. Corp., 283 F.3d 254, 267 (5th Cir. 2002)).

157. The relevant party to be warned is the prescriber rather than the actual patient who takes the prescription drug, unless the manufacturer knows or has reason to know that the prescriber is not in a position to reduce the

absolves suppliers of medical prescriptions of any duty to warn patients, so long as the suppliers have given the prescribing doctor sufficient warning of the drug's potential dangers. The physician thereby acts as an intermediary "between the company and the patient in protecting the patient and in providing direct information about the drug to the patient."<sup>158</sup> According to this theory, the physician, rather than the patient, understands which pharmaceutical is best for the patient, bearing in mind the patient's particular background, medical history, and other medications. The physician is therefore the person to whom any warnings should be directed.<sup>159</sup> Patients do not have the proper medical background to select their own medications—the selection and understanding of any particular medication requires understanding and training, and that necessitates the intervention of a physician.<sup>160</sup>

### B. *The Package Insert Should not be the Sole Focus*

In most failure-to-warn cases, the court resolves the adequacy-of-warning issue by focusing exclusively, or all but exclusively, on the package insert. This focus is neither required by the restatement nor called-for, in view of the realities of communication about warnings. And, as set out below, warning information about pharmaceuticals comes to physicians through a variety of sources—first and foremost through sources such as the Physicians' Desk Reference ("PDR"), a reference book containing the prescription drugs' labels exactly as they were approved by the FDA.<sup>161</sup> Physicians also receive direct mail from pharmaceutical companies including "Dear Doctor" letters, and package inserts that also state the warnings, side effects, and other information about each pharmaceutical.<sup>162</sup>

#### 1. Focus on the Package Insert Ignores the Warning-Diluting Information that Reaches Physicians through Pharmaceutical Marketing

As described above, pharmaceutical company representatives offer physicians lunches and copious amounts of information. The examples of pharmaceutical representatives downplaying warnings during these meetings are numerous, and further examples

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risk according to the label. RESTATEMENT (THIRD) OF TORTS: PRODUCT LIABILITY § 6(d)(2) (1998).

158. *MacPherson v. Searle & Co.*, 775 F. Supp. 417, 422-23 (quoting WILLIAM J. CURRAN, MARK A. HALL & DAVOID H. KAYE, *HEALTH CARE LAW, FORENSIC SCIENCE, AND PUBLIC POLICY* (4th ed. 1990)). *See also* Dietz v. Smithkline Beecham Corp., 598 F.3d 812, 815 (11th Cir. 2010) (explaining that the physician "has a duty to warn the patient's doctor, who acts as a learned intermediary between the patient and the manufacturer").

159. *See, e.g.*, *Seley v. G.D. Searle & Co.*, 423 N.E.2d 831 (Ohio 1981).

160. *Martin v. Ortho Pharm. Corp.*, 661 N.E.2d 352, 354 (Ohio 1996) (noting that "[p]rescription drugs are likely to be complex medicines, esoteric in formula and varied in effect. As a medical expert, the prescribing physician can take into account the propensities of the drug as well as the susceptibilities of his patient. His is the task of weighing the benefits of any medication against its potential dangers. The choice he makes is an informed one . . .").

161. *See* Foreword to PHYSICIANS' DESK REFERENCE (59th ed. 2005). The PDR also includes "indications, hazards, contraindications, side effects, and precautions" for each entry. *Id.* (quoting 21 C.F.R. §201.100(d)(1) (2005)).

162. FDA Draft Guidance for Industry, *Dear Health Care Provider Letters: Improving Communication of Important Safety Information*, FDA (issued Nov. 12, 2010), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM233769.pdf> ("Dear Doctor" letters inform doctors and other health care providers about information that "could affect the decision to use a drug or require some change in behavior by health care practitioners, patients, or caregivers to reduce the potential for harm from a drug").



come to light on a near-constant basis.<sup>163</sup> Yet the warnings that the court considers in a failure-to-warn lawsuit are most often limited to those contained in the package insert.<sup>164</sup> Despite a multi-billion-dollar marketing effort, many courts consider a properly worded package insert to be complete insulation from failure-to-warn liability, if combined with a proper entry in the PDR.<sup>165</sup> Courts have repeatedly held that where written warnings such as the package insert include the condition suffered by the plaintiff, the warnings are sufficient as a matter of law.<sup>166</sup>

This focus on the package insert is not helpful in assessing the information actually communicated between the pharmaceutical company and the physician because it does not take into account the reality of those communications, and the entirety of information that is actually viewed and considered by physicians. Although pharmaceutical companies must by law provide a package insert with their pharmaceuticals, they give physicians information in various other forms, as described above. While the package insert information, which also appears in the Physicians' Desk Reference, may reach physicians and alter their prescribing decisions, the promotional information provided by pharmaceutical companies is proven to reach physicians, as described above, and is documented to be effective in shaping physicians' prescribing decisions. Focus on the package insert is counter to the way information about drugs is communicated on the ground.

While pharmaceutical representatives are highly effective in reaching physicians with their marketing information, the same is not true of the package insert.

***The package insert is not user-friendly.*** As an initial matter, the package insert can contain information on many side effects, with little indication of how common they are. The package insert can contain an overload of information, rendering it difficult to use.<sup>167</sup> Package inserts have increased in length more than five-fold over the past twenty-five years; if printed on 8.5 by 11-inch paper, a package insert for one drug, Cisapride, would

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163. See discussion *supra* Part I.B.

164. See, e.g., *infra* note 165.

165. See, e.g., *Foister v. Purdue Pharm. L.P.*, 295 F. Supp. 2d 693, 705-08 (E.D. Ky. 2003); *MacPherson v. Searle & Co.*, 775 F. Supp. 417, 425 (D.C. 1991); *Weinberger v. Bristol-Myers Co.*, 652 F. Supp. 187, 190 (D. Md. 1986); *Dunkin v. Syntex Labs., Inc.*, 443 F. Supp. 121, 124 (W.D. Tenn. 1977); *Jacobs v. Dista Prods. Co.*, 693 F. Supp. 1029, 1032 (D. Wy. 1988) (granting summary judgment where warning stated potentially "life-threatening" side effect was reported and indicted the primary cause and management of it); *Caveny v. Ciba-Geigy Corp.*, 818 F. Supp. 1404, 1405 (D. Colo. 1992) (granting summary judgment where package insert noted a "causal relationship [was] probable"). Summary judgment is less likely to be granted where the package insert's language is equivocal or incomplete, but the focus remains on the package insert nonetheless. See, e.g., *Thom v. Bristol-Myers Squibb Co.*, 353 F.3d 848, 853 (10th Cir. 2003) (reversing summary judgment for defendant where package insert's warnings were equivocal and noting that a package insert's mere reference to a side effect is not necessarily an adequate warning); *Williams v. Lederle Labs.*, 591 F. Supp. 381, 385 (S.D. Ohio 1984) (denying summary judgment where package insert did not convey dangers sufficiently, was reluctant in tone, and had no sense of urgency); *Tongate v. Wyeth Labs.*, 580 N.E.2d 1220, 1224 (Ill. App. 1990) (denying summary judgment where warnings noted only that certain side effects were "reported" and "temporally associated" with the use of the drug and that a "causal relationship has not been established").

166. *Caveny*, 818 F. Supp. at 1404 (holding that package warnings were adequate as a matter of law where the warnings named aplastic anemia as a possible side effect and plaintiff died from that side effect; warnings did not have to state that medication was to be used only as a last resort); *Cather v. Catheter Tech. Corp.*, 753 F. Supp. 634 (S.D. Miss. 1991) (holding that package insert warnings were sufficient as a matter of law where warnings included venous thrombosis and embolism, which were the basis of plaintiff's complaint); *Martin v. Hacker*, 628 N.E.2d 1308 (N.Y. 1993) (holding that a package insert's warnings were sufficient as a matter of law where they warned of the very condition complained of by the plaintiff).

167. Raymond L. Woosley, *Drug Labeling Revisions—Guaranteed to Fail?*, 284 J. AM. MED. ASS'N 3047, 3048 (2000) ("In the last 25 years, the package inserts for new drugs have increased in length more than 5-fold.")

extend to more than ten pages.<sup>168</sup>

**The package insert is often unread.** The package insert often remains unread for purely practical reasons.<sup>169</sup> Because the package insert is, as the name suggests, provided in the pharmaceutical's packaging, the patient, rather than the physician, receives the package insert. The physician generally would have no reason to open up a pharmaceutical package and read the package insert. The same information that appears in the package insert does, however, appear in the Physicians' Desk Reference book, which exists in both print and online versions. However, physicians tend not to sit and read large sections of the PDR. Instead, the book is used as a reference guide to be consulted from time to time as questions arise.<sup>170</sup> Thus, when courts analyze the package insert and focus solely upon it, the analysis does not comport with the realities of the package insert and its ability to reach physicians.

The package insert's tendency to remain unread works in pharmaceutical companies' favor because of the causation requirement in a failure-to-warn claim. That is, in order to establish a failure-to-warn claim, a plaintiff must satisfy the element of causation.<sup>171</sup> The causation element in a failure-to-warn case requires that the inadequacy or absence of a warning must have caused the plaintiff's injury.<sup>172</sup> In most jurisdictions,<sup>173</sup>

168. *Id.* (noting also that the Cisapride package insert contains more than 470 facts about the drug).

169. *See, e.g.,* *Latiolais v. Merck & Co.*, 2008 WL 1723162, at \*1 (9th Cir. March 3, 2008) (affirming summary judgment because "Mr. Davis's physician testified that he neither read nor relied upon Zocor's labeling, including warnings, in prescribing it for Mr. Davis, and that even if the labeling had a prominent suicide warning he would still have prescribed it"); *Motus v. Pfizer Inc.*, 358 F.3d 659, 661 (9th Cir. 2003) (affirming summary judgment for defendant where physician testified that he had not read Zoloft's package insert, thereby establishing that the adequacy of these warnings was irrelevant); *In re Trasylol Prods. Liab. Litig.*, 2011 WL 2117257, at \*5 (S.D. Fla. May 23, 2011) (applying Ala. law) (noting "no record evidence indicating that [the prescriber] read the warning that Plaintiff claims was inadequate"); *Emody v. Medtronic, Inc.*, 238 F. Supp. 2d 1291, 1293, 1296 (N.D. Ala. 2003) (prescriber "did not even read the package insert"); *Gebhardt v. Mentor Corp.*, 15 Fed. App'x 540, 542 (9th Cir. 2001) (applying Ariz. law) ("evidence at trial showed that [the prescriber] did not read or rely upon the allegedly inadequate warnings of the [defendant's] device"); *Conte v. Wyeth, Inc.*, 85 Cal. Rptr.3d 299, 308 318-19 (Cal. Ct. App. 2008) ("[t]here can be no proximate cause where, as in this case, the prescribing physician did not read or rely upon the allegedly inadequate warnings promulgated by a defendant about a product"); *Lord v. Siqueiros*, 2006 WL 1510408, at \*3 (Cal. App. Dep't Super. Ct. Apr. 26, 2006) ("[prescriber] admits that he had not read the [drug's] label before prescribing it to the decedent"), *aff'd* 2007 WL 4418019, at \*4 (Cal App. Dec. 19, 2007) ("[prescriber] testified that he did not read the warning label prior to or after prescribing [the drug] to [plaintiff]"); *Stanback v. Parke, Davis & Co.*, 657 F.2d 642, 644 (4th Cir. 1981) ("[prescriber] had not read the package insert accompanying the vaccine"); *Douglas v. Bussabarger*, 438 P.2d 829, 831 (Wash. 1968) (prescriber "did not read the labeling which was on the container").

170. The Physicians' Desk Reference is "the most trusted and commonly used drug information reference." PDR, <http://www.pdr.net/about-pdr-network/> (last visited Nov. 27, 2013).

171. *Harris v. McHeil Pharm.*, 2000 WL 33339657, at \*4 (D.N.D. Sept. 5, 2000) (citing *Thomas v. Hoffman-LaRoche, Inc.*, 949 F.2d 806, 812 (5th Cir. 1992) ("To create a jury question, the evidence must be of sufficient weight to establish, by the preponderance of the evidence, at least some reasonable likelihood that an adequate warning would have prevented the plaintiff from receiving the drug.")).

172. *Thomas v. Hoffman-LaRoche, Inc.*, 949 F.2d 806, 812 (5th Cir. 1992) (applying Miss. law) (stating that "to create a jury question, the evidence introduced must be of sufficient weight to establish, by the preponderance of the evidence, at least some reasonable likelihood that an adequate warning would have prevented the plaintiff from receiving the drug"); *Motus v. Pfizer, Inc.*, 196 F. Supp. 2d 984, 991 (C.D. Cal. 2001) ("A plaintiff asserting causes of action based on a failure-to-warn must prove not only that no warning was provided or the warning was inadequate, but also that the inadequacy or absence of the warning caused the plaintiff's injury."); *Mazur v. Merck & Co.*, 742 F. Supp. 239, 262 (E.D. Pa. 1990) (noting that "[i]n the duty to warn context, assuming that plaintiffs have established both duty and failure-to-warn, plaintiffs must further establish proximate causation by showing that had defendant issued a proper warning to the learned intermediary, he would have altered his behavior and the injury would have been avoided.").

173. *Thomas*, 949 F.2d at 814 (noting that in some jurisdictions, a "heeding presumption" applies. This is a presumption that if an appropriate warning had been given, it would have been heeded. "Heeding" does not

the causation element requires that the plaintiff's physician must have actually read the inadequate warning.<sup>174</sup> The reasoning for this requirement is that if the physician did not read the warnings at all, a more suitable or adequate warning likewise would not have been read. An improved warning, therefore, would not have made any difference to the outcome, and its absence is not actionable.<sup>175</sup>

This outcome would make sense if the package insert were in fact the only information on safety and side effects that the pharmaceutical companies promulgate. That, as described above, is not the case.<sup>176</sup> In addition to the package insert, pharmaceutical companies promulgate a host of other statements regarding safety through their representatives and marketing materials. If, in keeping with this reality, the term "reasonable warning" were understood to consist of the package insert together with the pharmaceutical company's marketing statements regarding side effects and safety as well, then this causation element would be less likely to bar plaintiffs with failure-to-warn claims from reaching a jury.

In one case, for example, a physician testified that he had not read the Zoloft package insert; the court granted summary judgment, reasoning that proper warnings would have also remained unread.<sup>177</sup> The physician, though, had learned about Zoloft from Pfizer representatives, who recommended prescribing Zoloft for depression and panic attacks.<sup>178</sup> The representatives did not tell the physician about the relevant side effects of Zoloft, namely the increased risk of suicide.<sup>179</sup> As to many of the meetings with drug representatives, the physician could not remember exactly what was said or what was given to him, although the drug that he prescribed was a Pfizer sample.<sup>180</sup> This example shows in sharp relief why a focus on the package insert makes little sense—marketing information is devoid of any record, yet is reaching physicians. The package insert is a clear record and does not reach

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necessarily mean that a drug would not have been given, only that the prescriber would have "incorporated the 'additional' risk into [the] decisional calculus". *Id.* at 813 (using the drug may still be the less risky course of conduct); *see also* Talley v. Danek Med., Inc., 179 F.3d 154 163 (4th Cir. 1999). Thus, the heeding presumption is defeated if the physician testifies that communication of the enhanced warning would not have made a difference in the decision to prescribe. *See Stanbeck*, 256 F.3d at 1024 (affirming summary judgment for pharmaceutical company defendant where physician testified that she had independent knowledge of the allegedly absent warning and would have prescribed the drug even if given the additional warning information by the pharmaceutical company).

174. *See, e.g.*, Tucker v. Wright Med. Tech., Inc., 2013 WL 1149717, at \*17 (N.D. Cal. Mar. 19, 2013) (granting summary judgment for medical device defendant and finding inadequacy of warnings irrelevant where physician did not read warnings).

175. *Tucker*, 2013 WL 1149717, at \*16.

176. *See supra* Part I.

177. *Motus*, 196 F. Supp. 2d at 987.

178. *Id.* at 988.

179. *Id.* (noting that representatives did not tell the prescriber that Zoloft "could (1) cause akathisia; (2) worsen a patient's situation; (3) cause a patient to have suicidal thoughts; (4) cause a patient to experience a feeling so acute that death is a welcome result; or (5) increase the risk that a patient would commit suicide"); *see also* Lord v. Sigueiros, 2006 WL 1510408, at \*3-4 (Cal. App Dep't Super. Ct. April 26, 2006) ("[prescriber] admit[ted] that he had not read the [drug's] label before prescribing it to the decedent"; prescriber had heard information from pharmaceutical representatives but could not remember the substance of any discussions; overpromotion claim rejected), *aff'd* 2007 WL 4418019, at \*4 (Cal App. Ct. Dec. 19, 2007) ("[prescriber] testified that he did not read the warning label prior to or after prescribing [the drug] to [plaintiff]"); *Patterson v. AstraZeneca, LP*, 876 F. Supp. 2d 27, 36 (D.D.C. 2012) (noting that the physician could not remember any substantive information from any of the pharmaceutical representatives' thirty-one visits and concluding that the visits therefore had "little to no impact" on the physician).

180. *Motus*, 196 F. Supp. at 986.

physicians, yet its mere existence is decisive in many failure-to-warn cases.

## 2. Information about Pharmaceuticals is Dynamic While the Package Insert is Slow to Change

The package insert and the reality of a company's knowledge of side effects can be significantly out of step, with the warnings stating one position while the pharmaceutical representatives state another. This means that the reasonableness of the warning cannot be assessed without looking beyond the package insert.

Pharmaceutical companies must revise labeling as soon as there is "reasonable evidence" of a new, serious danger—a causal relationship need not have been proven.<sup>181</sup> Even when the updating process works as intended, the process can be laborious. In the case of Vioxx, for example, the company pursued an aggressive marketing campaign despite its knowledge of a link between Vioxx and an increased risk of heart attacks.<sup>182</sup> The evidence in litigation of failure-to-warn and other cases showed that Merck went to considerable lengths to avoid changing the package insert to include new warning information about cardiac risks, even though the risks were well known at the time.<sup>183</sup> The evidence at trial showed that Merck was aware of the cardiac risks even when Vioxx was first approved.<sup>184</sup>

The FDA called for further testing, but Merck did not do the testing right away. The company instead completed a large study known as the "VIGOR" study, which was performed on people with rheumatoid arthritis, with the goal of expanding the market for Vioxx. The study in fact confirmed the increased cardio-vascular risks. When Merck sought the new indication for Vioxx, Merck "sought to dilute the labeling required as a result of [its] VIGOR study" and "engaged in strenuous efforts to ensure that the results of the VIGOR study were not communicated to prescribing physicians by sales persons."<sup>185</sup> When the FDA was finally made aware of definitive evidence of increased risks, it took over two years for the labeling changes to occur.<sup>186</sup> The package insert, the company's knowledge about the risks, and the message that the company is promoting about the risks can differ from one another significantly. For this reason, in a failure-to-warn case, the package insert is just one example of the information the company is receiving, and the package insert likely does not reflect the company's complete knowledge at that time, or the message that pharmaceutical representatives are communicating on the ground.

## 3. While the Package Insert is Easily Available, Marketing Information is Often Unavailable as Evidence

The package insert is an appealing piece of evidence because it is readily available and its content is clear—other information may be unavailable. Pharmaceutical representatives' statements to physicians, for example, are often not available as evidence. These

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181. 21 C.F.R. §201.57(c) ("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; a causal relationship need not have been proved.")

182. *McDarby v. Merck*, 949 A.2d 223, 256 (N.J. Super. Ct. App. Div. 2008).

183. *Id.*

184. *Id.* at 259.

185. *Id.*

186. *Id.*

statements regarding warnings are most often made in private, are generally undocumented, and, therefore, can rarely be produced in litigation. Even those made at presentations or during physician events may not be documented. In a few celebrated cases, training materials have slipped out, resulting in shock and amazement at companies' directives to their pharmaceutical representatives.<sup>187</sup>

Often, faulty memory and an absence of documentation are the culprits. In fact, a brief review of published cases revealed case after case in which the package insert is in evidence, but parties to the conversation between pharmaceutical representative and physician cannot be remembered.<sup>188</sup> In these cases, the court may have considered the effect of pharmaceutical representatives' statements to physicians, but the court was unable to do so, given their unavailability. Courts are left, therefore, with the clear evidence of the package insert, which is often not read, and shadowy statements by pharmaceutical representatives, which are effective but undocumented. Under these circumstances, pharmaceutical cases tend not to even reach a jury.

#### 4. Exclusive Focus on the Package Insert Elevates the Regulations to De Facto Preemptive Status

The statutes governing FDA actions do not state that they preempt state failure-to-warn law, nor does the Restatement (Third) of Torts require that courts focus solely on the package insert when assessing warning information. To be sure, the FDA has at times pushed for such preemption in a marked departure from its previous stance on the issue.<sup>189</sup> Its efforts to date, however, have been rebuffed in the courts.<sup>190</sup> When courts considering failure-to-warn cases consider the package insert as sole and sufficient to amount to a "reasonable warning," courts are effectively deciding the preemption issue and according de facto preemptive status to the FDA regulations.

While a complete discussion of the merits of FDA preemption is beyond the scope of this article, suffice it to say that FDA regulation and the tort liability scheme serve two very different functions. The regulatory scheme developed by the FDA attempts to ensure safety by examining data about clinical trials performed by pharmaceutical companies, reviewing New Drug Applications by companies seeking to sell new pharmaceuticals, and requiring a detailed package insert for each pharmaceutical. The FDA's efforts, therefore,

187. See *supra* Part I.B.

188. See, e.g., *Prather v. Abbott Labs.*, 960 F. Supp. 2d 700, 716 (W.D. Ky. 2013) (noting in a medical device products liability lawsuit that the physician could not recall whether the representative explained how to use the medical device in question); *Dobbs v. Wyeth Pharm.*, 848 F. Supp. 2d 1335, 1338 (W.D. Okla. 2012) (noting, in a fraudulent misrepresentation lawsuit against a pharmaceutical company, that the physician "did not recall" receiving any specific information about the pharmaceutical in question); *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 255 (E.D.N.Y. 2007) (describing physician's testimony that he did not recall whether a pharmaceutical representative gave him warnings information about the weight gain associated with the drug Zyprexa).

189. David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims*, 96 GEO. L.J. 461, 463 (2008) (noting that "[t]he past few years have been marked by a seismic shift in FDA policy. The agency now maintains that state-law failure-to-warn cases threaten its ability to protect the public health. According to the agency, a determination in civil litigation that an FDA-approved label fails adequately to warn of risks may force manufacturers to add warnings that are not approved by the FDA, thus rendering the product 'misbranded'").

190. See generally *Wyeth v. Levine*, 555 U.S. 555 (2013).

are largely forward-looking. In addition, the FDA regulations can be seen as setting minimum standards.<sup>191</sup>

The toxic tort liability system, however, takes into evidence how the regulations set out by the FDA are actually followed in an individual case. In addition, tort law compensates those who are affected when the regulations do not work or when companies flout the rules.

A growing movement, represented by some state laws and, at one point, FDA's commentary on its regulations, urges a rebuttable presumption that a package insert compliant with FDA regulations preempts liability for failure-to-warn.<sup>192</sup> This movement, however, is still just that.<sup>193</sup> The New Jersey Supreme Court stated, for example, that compliance with FDA marketing and labeling specifications should mean "pharmaceutical manufacturers should not have to confront state tort liability premised on theories of design defect or warning inadequacy."<sup>194</sup> Compliance with all marketing requirements is extremely difficult to establish, however, so this approach quickly devolves into an exclusive focus on the label, as it did in the *Perez* case: Thus, "[a]ny duty to warn physicians about prescription drug dangers is presumptively met by compliance with federal labeling."<sup>195</sup> While the court noted that the presumption was not absolute, it allowed the presumption to be overcome only in the case of the manufacturer's "deliberate concealment . . . of after-acquired knowledge of harmful effects . . ."<sup>196</sup> Courts applying this standard have limited its application, noting that the FDA has a limited ability to find unforeseen post-approval side effects and that its oversight is flawed.<sup>197</sup>

Other courts have held that a package insert complying with FDA regulations is sufficient as a matter of law.<sup>198</sup> This approach, however, makes the FDA regulatory process presumptively preemptive of the court's full analysis in a failure-to-warn case. Preemption is not currently the law, and it should not become the law in a back-door manner through

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191. *Rite Aid Corp. v. Levy-Gray*, 876 A.2d 115, 132 (Md. App. 2005) (citing *Graham v. Wyeth Labs.*, 666 F. Supp. 1483, 1491 (D. Kan. 1987) ("FDA regulations of prescription drugs are generally viewed as setting minimum standards, both as to design and warning.")).

192. N.J. STAT. ANN. § 2A:58C-4 ("If the warning or instruction given in connection with a drug or device or food or food additive has been approved or prescribed by the federal Food and Drug Administration under the 'Federal Food, Drug, and Cosmetic Act,' 21 U.S.C. § 301 et seq. or the 'Public Health Service Act,' 42 U.S.C. § 201 et seq., a rebuttable presumption shall arise that the warning or instruction is adequate.").

193. The FDA stated in a preamble to a 2006 rule meant to revise drug labeling requirements that "FDA approval of labeling . . . preempts conflicting or contrary State law." 71 Fed. Reg. 3922, 3934-35 (2006).

194. *Perez v. Wyeth Labs., Inc.*, 734 A.2d 1245, 1257 (N.J. 1999).

195. *Id.* at 1259.

196. *Id.*

197. *McDarby v. Merck*, 949 A.2d 223, 256-57 (N.J. 2008).

[S]crutiny disclosed flaws in the regulatory system, existing at least until the time of the 2007 Amendments, that render the dictum of *Perez* less all-encompassing than it might then have appeared. Commentators and courts have since recognized that, whereas pre-market approvals of drugs are generally thorough in nature, the ability of the FDA, post-market, 'to detect unforeseen adverse effects of [a] drug and to take prompt and effective remedial action' is considerably less . . . . It is these flaws in that post-marketing oversight process that provide the foundation for the further exception to the presumption of adequacy that we find applicable to this case.

*Id.*

198. *Hurley v. Lederle Labs.*, 863 F.2d 1173 (5th Cir. 1988) (explaining that the FDA extensively reviews the warnings and information from the pharmaceutical company and that when the FDA approves the warning, the company must use that exact warning; to require another warning under state law would conflict with the FDA).

a narrow focus on the package insert.

C. *The “Overpromotion” Exception to the Learned Intermediary Defense is Inadequate, Because the Bar is Impossibly High*

Occasionally, direct and clear evidence of pharmaceutical representatives’ down-playing of warnings is available as evidence. In these situations, courts are sometimes receptive to the argument that warnings can hardly function as such when they are being undermined by intense marketing efforts. Indeed, for decades, some courts have suspected the influence of marketing efforts on physicians’ decision-making and have therefore shown willingness to consider pharmaceutical representatives’ statements as part of a failure-to-warn case.

The seeds of a claim for negligent overpromotion of a drug or chemical appeared in a 1974 North Carolina case in which a child died of aplastic anemia after receiving a drug prescribed by her physician.<sup>199</sup> The subsequent lawsuit claimed that the drug company improperly marketed the drug, overpromoted the drug to physicians, and did not provide physicians with proper warnings.<sup>200</sup> Reversing summary judgment for the defendant, the court explained that simply following the letter of the law could be an insufficient shield against liability if the drug had been overpromoted.<sup>201</sup> A California court denied summary judgment, likewise agreeing that overpromotion of a drug could have overcome the package insert’s warnings of the blood dyscrasia with certain uses of the drug; the pharmaceutical company had provided calendars and other gifts, such that physicians could have been influenced to prescribe the drug where they might not otherwise have done so.<sup>202</sup>

More recently, a federal district court in Ohio agreed that overpromotion could nullify even otherwise sufficient warnings.<sup>203</sup> A New York court agreed that “[i]n unusual cases, courts have found a drug manufacturer’s excessive promotion of its product may negate or call into question operation of the learned intermediary doctrine.”<sup>204</sup>

To establish this exception to the learned intermediary defense, courts currently require a showing “that such overpromotion caused the physician to initiate or maintain the prescription at issue. General claims of overpromotion are not sufficient.”<sup>205</sup> Only in rare

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199. *Whitely v. Cubberly*, 210 S.E.2d 289 (N.C. Ct. App. 1974).

200. *Id.*

201. *Id.* at 292 (noting “that Parke, Davis may have fully complied with all applicable Federal laws in its marketing and labeling Chloromycetin would not in itself free it of liability for harm caused by use of the drug if it were shown that such use and resulting harm was caused by the company’s negligent acts in overpromoting the drug, the dangerous properties of which it was aware or in the exercise of due care should have been aware.”).

202. *Stevens v. Parke, Davis & Co.*, 507 P.2d 653 (Cal. 1973).

203. *In re Meridia Prods. Liab. Litig.*, 328 F. Supp. 2d 791, 814 (N.D. Ohio 2004) (granting summary judgment for defendant pharmaceutical manufacturers but noting that “[h]ad they come forth with evidence that using Meridia poses substantial risks of harm, then their claims that overpromotion nullified the defendants’ workings might have been sufficient. Given the paucity of evidence that Meridia is harmful, however, the Court must reject this claim.”).

204. *In re Zyprexa Prods. Liab. Litig.*, 2009 WL 2004540, at \*14 (E.D.N.Y. July 1, 2009); *see also* *Dean v. Eli Lilly & Co.*, 387 Fed. App’x 28, 30 (2d Cir. 2010) (quoting *Beale v. Biomet, Inc.*, 492 F. Supp. 2d 1360, 1377 (S.D. Fla. 2007) (noting that with this exception “overpromotion of a product negates any warnings . . . such that a manufacturer of the product cannot avail itself of the doctrine”).

205. *In re Zyprexa Prods. Liab. Litig.*, 649 F. Supp. 2d 18, 33 (E.D.N.Y. 2009). “In order to defeat a motion for summary judgment, an assertion of overpromotion must be well-supported factually.” *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 268 (E.D.N.Y. 2007).

cases, however, is the overpromotion exception successful.<sup>206</sup>

The exception is difficult to establish in part because the evidence is so hard to find. Unlike the package insert, which is memorialized and easily accessible, evidence of overpromotion or watering down occurs in private conversations or at social events, which are difficult, if not impossible to reconstruct and bring into court. Again and again, courts reject an overpromotion claim due to lack of any concrete evidence:

- Where a pharmaceutical representative visited a physician thirty-one times, the physician prescribed the medication in question and then failed to recognize a warned-of side-effect in the patient, there was no “concrete evidence” of overpromotion. The court required—but could not find—“a link between these visits and misinformation that would make the prior warnings ineffective.”<sup>207</sup>
- Despite a “vigorous sales campaign” aimed at the physician in question, there was “no evidence that [the manufacturer’s] sales people either misled [the physician] about the link between Zyprexa and diabetes or caused [the physician] to prescribe Zyprexa to [plaintiff]”<sup>208</sup>
- Summary judgment for defendants where plaintiff did not show that “Biomet’s marketing materials [] induce[d] him to inappropriately select patients for the device.”<sup>209</sup> Marketing “included sales visits to surgeons, advertisements in orthopedic journals, presentations at meetings of orthopedic surgeons, video demonstrations and literature about the product. Biomet also sponsored articles written about its product.”<sup>210</sup>

The overpromotion exception shows that courts are cognizant of pharmaceutical marketing’s realities—that is, that alongside the printed warnings there exists a far more compelling universe of marketing materials and presentations that can effectively undo the very warnings that were given. In addition, studies establish that the marketing often drives the decision to prescribe.<sup>211</sup>

But the overpromotion exception has proven ineffective to take account of these anti-warnings because it requires a showing that is all but impossible for plaintiffs to provide. Courts apply the following standard, based on the marketing’s *actually causing* the

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206. *Incollongo v. Ewing*, 282 A.2d 206 (Pa. 1971) (holding that evidence that a sales force has “minimized the dangers of [a] drug while emphasizing its effectiveness, wide acceptance and use, and lack of certain objectionable side effects associated with other drugs” was sufficient to suggest that the “printed words of warning were in effect cancelled out and rendered meaningless”).

207. *Patteson v. AstraZeneca, LP*, 876 F. Supp. 2d 27, 36 (D.D.C. 2012). *Contra Holley v. Burroughs Wellcome Co.*, 348 S.E.2d 772 (N.C. 1986) (noting that plaintiff’s overpromotion claim had support sufficient to defeat defendant’s motion for summary judgment).

208. *Dean v. Eli Lilly & Co.*, 387 Fed. App’x. 28, 30 (2d Cir. 2010).

209. *Beale v. Biomet, Inc.*, 492 F. Supp. 2d 1360, 1377-78 (S.D. Fla. 2007).

210. *Id.* at 1363.

211. *See supra* Part I.



prescribing decision: “That such overpromotion caused the physician to initiate or maintain the prescription at issue. General claims of overpromotion are not sufficient.”<sup>212</sup> That is, the overpromotion exception usually proceeds in two steps—first, the analysis of the warning and a finding that it meets the “reasonableness” standard, and then, in a distinct and separate step, whether the alleged overpromotion caused the physician to prescribe the drug in question.<sup>213</sup>

As a practical matter, this standard is all but impossible to meet. Recall that even physicians themselves do not believe pharmaceutical representatives have an effect on their decision-making, even though empirical studies show that they do.<sup>214</sup> The evidence that courts require could consist of a physician testifying that when he or she received a pharmaceutical company stipend or attended a dinner, his or her professional judgment was affected. A physician could testify that he or she had responded to a pharmaceutical representative’s request that his or her “next four” prescriptions be for that representative’s products, as pharmaceutical representatives are known to have requested.<sup>215</sup> Such testimony, however, is difficult to imagine and would surely be rare at best. Perhaps for these reasons, the overpromotion exception has failed repeatedly to the point that it is generally an empty gesture. The overpromotion exception is inadequate to address the vigorous marketing that has become routine in the pharmaceutical industry.

A physician’s decision-making with regard to warnings is therefore affected by warning-related information from a number of sources, not just the package insert. Because the physician’s judgment is based on the package insert plus assurances from pharmaceutical representatives, these other statements and assurances from pharmaceutical representatives should be included in the warnings as part of a failure-to-warn case.

#### IV. TOTAL MIX: THE FAILURE-TO-WARN ANALYSIS SHOULD CONSIDER ALL OF THE PHARMACEUTICAL COMPANY’S WARNING AND WARNING-DILUTING INFORMATION

When pharmaceutical marketing is recognized for what it is—a significant yet surreptitious factor in many prescribing decisions—the failure-to-warn analysis must change accordingly, in at least the following three ways, described in more detail below: (1) in analyzing the reasonableness of a warning, courts should not consider the package insert in isolation; courts should consider *all* of the pharmaceutical company’s warning or warning-diluting statements that reach physicians through pharmaceutical marketing; (2) in the causation analysis, a physician’s failure to read the package insert should not, alone, be sufficient to defeat causation; (3) finally, research demonstrates that social psychology operates at a subconscious level, so a physician’s own statement that pharmaceutical marketing did not affect the prescribing decision should not be conclusive—a jury should be able to decide for itself the effect of pharmaceutical marketing in a particular case.

##### A. *Courts Analyzing the Reasonableness of a Warning Should Consider the Full Spectrum of Warning and Anti-Warning Information that Reaches Physicians—Not*

212. *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d at 268.

213. *See supra* notes 207-98.

214. *See supra* Part I.

215. *See supra* Part I.

*Just the Package Insert*

As explained above, the package insert has become the go-to piece of information in a pharmaceutical failure-to-warn case, often serving as the beginning and end of the warnings analysis.<sup>216</sup> But consideration of all the warnings information would be in harmony with criteria that have been used by various courts in the past. A reasonableness analysis has included the following factors, although courts have often focused on particular factors to the exclusion of others or ignored them entirely in favor of the package insert: (1) the warning must state the significant risks involved and be factually correct<sup>217</sup>; (2) the warning must have the physical attributes such that a reasonably prudent person would be alerted to the dangers; (3) the warning must communicate the seriousness of the harm that may result; (4) the warning cannot be ambiguous, equivocal, or contradictory;<sup>218</sup> (5) the warning should be easily understood by the intended audience; and (6) the warning should be communicated by the most appropriate means.<sup>219</sup> The mere mention of a possible injury or side effect may not be adequate.<sup>220</sup>

Information from pharmaceutical representatives that downplays or contradicts written warnings would fall afoul of factor number four, the requirement that the warnings be unequivocal. That is, even if the package insert does state the warnings information, that information is undercut by contradictory information provided by pharmaceutical representatives.

Instead of a weak “overpromotion” exception, therefore, today’s pharmaceutical marketing requires that courts instead consider marketing materials and statements in the first instance. That is, the marketing statements made to physicians should be considered alongside the warning language, to see whether the warning is “reasonable” in its entirety. The information would be placed together with the warning information that pharmaceutical companies provide to physicians: both warnings *and* warning-diluting information

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216. *Supra* note 165.

217. *See* Jackson v. Johns-Manville Sales Corp., 750 F.2d 1314, 1320 (5th Cir. 1985); Deines v. Vermeer Mfg. Co., 755 F. Supp. 350, 353 (D. Kan. 1990) (“The manufacturer’s duty is to warn of all potential dangers which it knew, or in the exercise of reasonable care should have known, to exist.”); *In re Meridia*, 328 F. Supp. 2d at 812 (citing Pittman v. Upjohn Co., 890 S.W.2d 425, 429 (Tenn. 1994) (holding that a pharmaceutical company’s warning to physicians is adequate if it “contain[s] a full and complete disclosure of the potential adverse reactions to the drug”); Seley v. G.D. Searle & Co., 423 N.E.2d 831 (Ohio 1981) (“A warning is adequate . . . where, under all the circumstances, it reasonably discloses to the medical profession all risks inherent in the use of the drug which the manufacturer knew or should have known to exist.”).

218. *See, e.g.*, Salmon v. Park, Davis & Co., 520 F.2d 1359 at 1363 (4th Cir. 2012) (statement expressing doubt about causal connection between chloramphenicol and aplastic anemia diluted a disclosure stating the need to take precautions against anemia); Givens v. Lederle, 556 F.2d 1341, 1345 (5th Cir. 1977) (a warning for an oral polio vaccine was potentially inadequate where it stated the risk of paralysis as one in three million but then cast doubt on the causal link between the vaccine and the paralysis). As explained in further detail in Part III.B, a warning may also be diluted by subsequent advertising and promotional activities which downplays the product’s risks. *See* Stevens v. Parke, Davis & Co., 507 P.2d 653, 662 (Cal. 1973) (warning provided to physicians by drug company about the risk of aplastic anemia from administration of Chloromycetin antibiotic to patients was nullified by subsequent overpromotion); *Incolligo v. Ewing*, 282 A.2d 206, 220 (Pa. 1971) (warning provided to physicians by drug company about the risk of aplastic anemia from administration of Chloromycetin antibiotic to patients was nullified by subsequent overpromotion).

219. *Id.*

220. *In re Meridia*, 328 F. Supp. 2d at 812 (citing Stahl v. Novartis Pharm. Corp., 283 F.3d 254, 267 (5th Cir. 2002)).

should be considered as part of the “reasonable warning” analysis cited in the Restatement.<sup>221</sup>

One practical result of this analysis would be that a greater number of claims survive summary judgment and potentially reach a jury. If a court considers the package insert alone, the result is often summary judgment for the defendant.<sup>222</sup> This is because an unambiguous warning is considered a question of law for the court to decide.<sup>223</sup> The package insert, considered alone, often states every possible side effect and gives all the warning information, so considered in isolation, it is often an unambiguous warning. Consideration of contradictory evidence concerning warnings, such as some of the information from pharmaceutical representatives, could well render the warning ambiguous—an ambiguous or contradictory warning is a question of fact suitable for a jury to decide.<sup>224</sup> Summary judgment on a warning’s adequacy is not appropriate where the warning does not convey “a fair indication of the nature of the dangers involved, was reluctant and equivocal in tone, and lacked a sense of urgency.”<sup>225</sup>

The consideration of pharmaceutical marketing information as part of the warnings will no doubt be met with some criticism. It could be argued, for example, that physicians are held to a professional standard of care that calls for them to be aware of the proper instructions for medications they prescribe, and that they should therefore read the package insert regardless of any marketing.<sup>226</sup> Arguably, they should be capable of reading and digesting a package insert and ignoring all other information that might dilute or otherwise neutralize the package insert’s warnings. While physicians are, of course, charged with following the standard of care, such an argument improperly merges a failure-to-warn claim with a malpractice claim. That is, the time to analyze a physician’s adherence to the standard of care is when the physician’s actions towards the patient are at issue. In a failure-to-warn claim, however, the pharmaceutical company’s actions are at issue and the focus should remain on those actions. In addition, to assume that physicians focus only on the package insert is to ignore the documented effects of pharmaceutical marketing.

Furthermore, this approach could result in higher settlements for plaintiffs and potentially increase judgments against pharmaceutical companies because additional cases

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221. RESTATEMENT (THIRD) OF TORTS § 6(d) (1998).

222. *See supra* Part III.B.

223. *See, e.g.,* *Tongate v. Wyeth Labs.*, 580 N.E.2d 1220, 1224 (Ill. App. 1991) (“[T]he adequacy of warnings is a question of fact, not law, for the jury to determine . . . .”); *Martin v. Hacker*, 628 N.E.2d 1308 (N.Y. 1993) (“In determining whether a warning is adequate as a matter of law or presents a question of fact for the jury, New York courts ‘evaluate the [warning]’s language for its accuracy, clarity and relative consistency.’ The sufficiency of the warning can become a question of law where the warning is clear, accurate and unambiguous”); *Hernandez v. Schering Corp.*, 958 N.E.2d 447, 455 (Ill. App. 2011) (citing *Upjohn Co. v. MacMurdo*, 562 So.2d 680 (Fla. 1990)); *Kelso v. Bayer Corp.*, 398 F.3d 640 (7th Cir. 2005) (applying Ill. law).

224. *See, e.g.,* *Tongate*, 580 N.E.2d at 1220.

225. Michael Imbrosio, *Adequate Warnings in the Face of Uncertain Causality: The Learned Intermediary Doctrine and the Need for Clarity*, 107 W. VA. L. REV. 847, 852 (2005) (quoting *Williams v. Lederle Labs.*, 592 F. Supp. 381, 385 (S.D. Ohio 1984)).

226. The FDA approved labeling is often used to establish a standard of care for correct use of a medication, either with or without expert testimony. Bill Vaslas & Neil Schreffler, *The Role of FDA-Approved Labeling in Medical Malpractice Litigation*, PDR NETWORK, available at [http://www.pdrnetwork.com/docs/default-source/educational-materials/novdec2010\\_22-26vaslas\\_schreffler.pdf?sfvrsn=2](http://www.pdrnetwork.com/docs/default-source/educational-materials/novdec2010_22-26vaslas_schreffler.pdf?sfvrsn=2) (last visited August 29, 2013) (noting approaches by which the FDA Labeling is recognized as prima facie evidence of the standard of care sufficient for submission to a jury—the “Mulder rule”—as opposed to other approaches by which the FDA Labeling must be accompanied by expert testimony to establish the standard of care).

would survive summary judgment. Some would argue that this could result in increased costs of pharmaceuticals for patients, and that the approach proposed in this article therefore should not be adopted.<sup>227</sup> Costs of pharmaceutical litigation are already significant.<sup>228</sup> Nevertheless, litigation serves an important function, given that the FDA cannot detect and prevent every safety-related problem.<sup>229</sup> Indeed, some commentators argue that the pendulum has swung too far toward the criticism of litigation's "over-deterrent" influence, such that legislation, case law, and scholarship have turned away from the idea that products liability improves consumer welfare.

To dissuade pharmaceutical representatives from undercutting written warnings, all the information that doctors receive should be considered. A "warning" cannot be effective if it is undercut by additional information and assurances—from the same pharmaceutical company source as the package insert—that attempt to discount legitimate fears or neutralize otherwise effective warnings.

*B. In the Causation Analysis, a Physician's Failure to Read the Package Insert Alone Should not be Sufficient to Defeat Causation*

As explained above,<sup>230</sup> where a physician does not read a package insert, courts frequently grant summary judgment, reasoning that if the physician did not read the extant warnings, additional or stronger warnings would not have made any difference because the physician would not have read those either.<sup>231</sup>

The problem with this analysis is that it does not take into account the surreptitious effects of pharmaceutical marketing. That is, where the physician has been the target of a marketing campaign regarding the drug at issue, summary judgment is inappropriate because research shows that when pharmaceutical marketing targets physicians, the marketing dilutes warnings in the package insert (which tends not to be read anyway) and replaces those FDA-vetted warnings with statements that either downplay the warnings or eliminate them completely.<sup>232</sup> As explained above, targeted physicians tend to select the marketed drug both when it is indicated in the warning and when it is not.<sup>233</sup>

Thus, before concluding that a physician took in *no* warning information, based purely on an unread package insert (and hence that better warnings would have made no

227. See, e.g., Schwartz, *supra* note 99, at 165-66 (discussing various disadvantages to litigation over approved drugs and warnings but assuming that the warning is composed only of the official warning).

228. See, e.g., David G. Owen, *Dangers in Prescription Drugs: Filling a Private Law Gap in the Healthcare Debate*, 42 CONN. L. REV. 733, 737 (2010) (noting the cost of pharmaceutical litigation, including settlements involving drugs such as Vioxx—settlement of 50,000 cases for \$4.85 billion— and Zyprexa —\$1.415 billion in civil and criminal penalties).

229. Anita Bernstein, *Enhancing Drug Effectiveness & Efficacy Through Personal Injury Litigation*, 15 J. L. POL'Y 1051, 1098-99 (2007).

230. See *supra* Part III.B.

231. *Motus, v. Pfizer*, 358 F.3d 659, 661 (9th Cir. 2004) (affirming district court's grant of summary judgment because the prescribing physician "did not read the warning label that accompanied Zoloft or rely on information provided by Pfizer's detail men before prescribing the drug to Mr. Motus . . .").

232. See, e.g., Barbara Mintzes, PhD, et al., *Pharmaceutical Sales Representatives and Patient Safety: A Comparative Prospective Study of Information Quality in Canada, France, and the United States*, *Health Policy*, 28(10) J. GEN. INTERN. MED. 1368, 1373 (2013) (noting that in all three countries studied, pharmaceutical representatives rarely informed physicians about serious adverse events and observing a "serious lack of information" in pharmaceutical representative discussions about medications).

233. Sah & Fugh-Berman, *supra* note 25.

difference), the court should determine whether the physician was exposed to marketing information on the drug in question. Marketing information is proven to move the decision-making needle when it reaches physicians, whether physicians realize it or not.<sup>234</sup>

C. *Social Psychology-Based Marketing Operates at a Subconscious Level, so a Physician's Own Statement on its Effects Should not be Conclusive as to the Causation Element*

Finally, research demonstrates that social psychology operates at a subconscious level, so a physician's own statement that pharmaceutical marketing did not affect the prescribing decision should not be conclusive—a jury should be able to decide the effect of pharmaceutical marketing in each case.

Marketing techniques based on social psychology operate at a subconscious level, so the targeted person is not the best judge of the techniques' effectiveness.<sup>235</sup> Indeed, physicians themselves have been demonstrated *not* to be the best judges of whether their decision-making was affected by pharmaceutical marketing.<sup>236</sup> The empirical research cited above indicates that physicians are affected by marketing, even though they are often confident that they are not affected.<sup>237</sup> In addition, they assessed marketing materials as accurate and sufficient to serve as the basis for a decision to prescribe, even when warnings were left out.<sup>238</sup>

When a physician testifies that he or she was not affected by pharmaceutical marketing and that proper warnings would have made no difference, some courts have granted summary judgment for the defendant pharmaceutical company, based on the absence of causation.<sup>239</sup> That is, the summary judgment can be based purely on the physician's own statement of what he or she would have done if the warning had been different.<sup>240</sup> If the physician testifies that he or she would have made the same decision to prescribe regardless of a different or better warning, then arguably the pharmaceutical company's failure to give a proper warning did not affect the decision to prescribe.

But a different outcome can—and should—result when there is reason to question the physician-witness's assessment. That is, when there is reason to question the conclu-

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234. *Id.*

235. *Id.*

236. *Id.*

237. *See supra* Part I.C.

238. Mintzes, *supra* note 232, at 1373 (noting that “[d]espite these omissions [of safety information], physicians judged information quality positively and expressed willingness to increase prescribing nearly two-thirds of the time.”).

239. *See, e.g.,* Motus v. Pfizer, 196 F. Supp. 2d 984, 997-98 (C.D. Cal. 2001) (basing summary judgment on physician's testimony that he met with pharmaceutical representatives and attended pharmaceutical company seminars but was not affected by any pharmaceutical company statements or materials); Stanback v. Parke, Davis & Co., 657 F.2d 642, 644-45 (4th Cir. 1981) (applying Va. law and granting summary judgment when physician testified that adequate warnings would not have changed a prescribing decision); Plummer v. Lederle Labs., 819 F.2d 349, 358 (2d Cir. 1987) (applying Cal. law); Windham v. Wyeth Labs., Inc., 786 F. Supp. 607, 612 (S.D. Miss. 1992) (applying Miss. law); Strumph v. Schering Corp., 626 A.2d 1090 (N.J. 1993) (applying N.J. law); Thomas v. Hoffman-LaRoche, Inc., 949 F.2d 806, 817 (5th Cir. 1992) (applying Miss. law).

240. *Supra* note 239.

siveness of a physician's after-the-fact assessment of what might have happened if a theoretical, more complete warning had been given.<sup>241</sup> Even without focusing on the surreptitious effects of pharmaceutical marketing, some courts have declined to grant summary judgment on causation where the physician testifies that a proper warning would not have made a difference in the decision to prescribe.<sup>242</sup> This issue, those courts explain, should present a jury question.<sup>243</sup>

Research shows that pharmaceutical marketing affects physicians, encouraging them to prefer certain medications over others and even prescribe when a medication is not indicated.<sup>244</sup> At the same time, the marketing is based on principles of social psychology, so that the targeted person is the least likely to realize the marketing's effects.<sup>245</sup> So, when there is evidence that the physician was the target of pharmaceutical marketing of the medication at issue, the jury should have the opportunity to decide how the marketing affected the physician's judgment and whether the marketing made a difference in the particular case. After all, the causation question concerns actual causation, rather than just one person's opinion of whether or not he or she was persuaded, particularly where research indicates the person may not be the most reliable judge of whether the persuasion was effective.

The assessment of causation should take into account the pervasive reach of pharmaceutical marketing, and the fact that by its very nature, pharmaceutical marketing skews the judgment of those it targets. A physician's judgment of what his or her decision would have been if faced, in the past, with a more complete warning, should not result in summary judgment. An outside party—the jury—should be able to determine the answer to that causation question.

## V. CONCLUSION

Pharmaceutical representatives' marketing to physicians is proven to affect physician decision-making, even without physicians realizing the effect. The analysis of a warning's reasonableness in the context of a failure-to-warn case should recognize the power of this marketing and that the package insert is not the only warnings-related information reaching physicians. Indeed, the loud and persistent marketing campaigns often drown out the scientific evidence, and result in the prescribing of medications that may not be appropriate for the patient, may not be the most cost-effective option, or may be downright

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241. *Doe v. Miles Labs., Inc.*, 927 F.2d 187, 195 n.32 (4th Cir. 1991) (applying Md. law and noting that although physician testified that she would have administered the drug in question even with full knowledge of the associated AIDS risk, this "hindsight opinion [was] not conclusive of what she would have done had she been invested with all pertinent facts regarding [the medication]. Thus, the causation issue . . . presents a genuine issue of material fact"); *Williams v. Lederle Labs.*, 591 F. Supp. 381, 387 (S.D. Ohio 1984) (applying Ohio law) ("What [the physician] might or might not have done involves to some degree his credibility. Thus, we conclude that it is for the jury to determine whether the presence of an adequate warning would have made no difference in [the physician's] decision"); *Strumph v. Schering Corp.*, 606 A.2d 1140, 1146-47 (N.J. Super. Ct. App. 1992) ("A well-prepared advocate may be able to erode at trial the physician's testimony [that the physician would have prescribed the drug even in the face of a proper warning]"); *Garside v. Osco Drug, Inc.*, 976 F.2d 77, 83 n.9 (1st Cir. 1992) (noting that even if physician's testimony had been unequivocal on the issue of what physician would have done if given the appropriate warning, Massachusetts courts would be reluctant to permit such after-the-fact speculation to insulate a pharmaceutical company from liability).

242. *Doe*, 927 F.2d at 195 n.32.

243. *Id.*

244. *Sah & Fugh-Berman*, *supra* note 25.

245. *Supra* note 23.

dangerous for the particular patient.

Courts' analysis of warnings material in the context of a failure-to-warn case should, at a minimum, keep pace with research showing the true breadth and influence of warnings—and warning-diluting—information actually reaching physicians.