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# Conflict of Interest, Bias, and Manipulation: Reassessing Prescriber Education and the Learned Intermediary Doctrine

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## Conflict of Interest, Bias, and Manipulation: Reassessing Prescriber Education and the Learned Intermediary Doctrine

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### Abstract

The purpose of this essay is to explore how the pharmaceutical industry's influence impacts the drug approval process and the resulting information provided by drug manufacturers to healthcare providers and ultimately to patients. For nearly half a century, United States courts have held under the Learned Intermediary Doctrine that the makers of prescription drugs are responsible for educating prescribers, not patients, about their products. The dialectic tension between corporate profits and required prescriber education calls into question the credibility of drug information from corporate, medical, and government sources. The key question to be addressed in this paper is, how credible is the information provided to prescribers by pharmaceutical manufacturers? Numerous critics have called into question the FDA's ability to assure that medical drugs are safe and effective and the communication about them is accurate and unbiased. But the FDA is not the only healthcare organization that collaborates with the pharmaceutical industry and creates confusion and perpetuates deceptions. Medical schools accept money for clinical trials, provide researchers, and cooperate with pharmaceutical manufacturers much to the concern of numerous critics. In addition, clinical trials data, publications, and continuing education frequently lack credibility related to researcher/author bias and conflicts of interest. Unless the influence of the pharmaceutical industry on contemporary healthcare is markedly altered or eliminated, prescribers cannot rely on the information they are provided and therefore should not be held liable by the courts as learned intermediaries.

### **Conflict of Interest, Bias, and Manipulation: Reassessing Prescriber Education and the Learned Intermediary Doctrine**

#### Introduction

“The profession of medicine, in every aspect—clinical, education, and research—has been inundated with profound influence from the pharmaceutical and medical device industries” (DeAngelis and Fontanrosa, 2008, p. 1833). This quote from an Editorial by the Editor and Executive Deputy Editor of the *Journal of the American Medical Association* succinctly describes the fundamental issue to be addressed by this paper. The purpose of this essay is to explore how the pharmaceutical industry's profound influence impacts the drug approval process and the resulting information provided by the pharmaceutical industry to healthcare providers and ultimately to patients.

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Every day millions of Americans are prescribed or take medications, seek treatments, and/or consult with their healthcare providers. These actions are primarily based on patients' assumptions that the information they receive from their providers and the treatment decisions they make are scientifically valid, clinically tested, and ethically grounded. Similarly, prescribers make treatment recommendations and decisions and provide information based on published data from clinical trials that they presume to be accurate, complete, and objectively scrutinized. In fact, healthcare providers' legal risks are based on their assimilation of that data and the prescriber's analyses of a product's efficacy and safety for an individual patient's condition or treatment.

For nearly half a century, United States courts have held that manufacturers of prescription drugs and medical devices are responsible for educating prescribers, not patients, about their products. This doctrine is perhaps most clearly defined by the Fifth Circuit Court of Appeals (1974) that stated:

prescription 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, an individualized medical judgment bottomed on a knowledge of both patient and palliative. Pharmaceutical companies then, who must warn ultimate purchasers of dangers inherent in patent drugs sold over the counter, in selling prescription drugs are required to warn only the prescribing physician, who acts as a "learned intermediary" between manufacturer and consumer. (*Reyes v. Wyeth Labs*, 498 F.2d 1264, 1276)

Based on this ruling and others, the onus is on prescribers to not only become educated about a prescription drug or device, but also to use that information to critically assess the safety and efficacy of the product for each individual patient. In addition, according to the doctrine, prescribers are expected to effectively educate their patients about the appropriateness, side effects and/or warnings, associated with a particular treatment.

The learned intermediary doctrine is a late twentieth century legal construct that was first argued in *Sterling Drug v. Cornish* (1966). According to Cooner (2003)

at its core, the doctrine is pragmatic: it recognizes that the warnings and instructions which accompany medicines and medical devices are directed not to the ultimate consumers or the end users of those products, but to the physicians who prescribe them and who are in the best position to evaluate the risks associated with their use. (para. 1)

This doctrine recognizes a prescriber's education, experience, and knowledge in prescribing medications or treatment. However, the doctrine also requires drug manufacturers to provide detailed product information to prescribers: physicians (MD/DO); physician assistants (PA); and advanced practice registered nurses (APRN) to help them determine how therapies will positively or negatively impact a patient's disease and/or wellness (Thornton, 2003). Based on the doctrine's apparent assumptions regarding the veracity and completeness of the data and information provided to prescribers, this essay seeks to examine the history of communication about prescription medications from pharmaceutical companies to learned intermediaries. To better understand the interdependent nature of the prescriber – pharmaceutical manufacturer relationship it is important to first examine the issue of drug treatment from a historical perspective.

Sir William Osler (1932) recognized the inherent problems for medical practitioners in trying to find safe and effective medications. In a speech at McGill Medical School in 1895, Osler stated, "of the difficulties inherent in the art not one is so serious as this which relates to the cure of disease by drug. There is so much uncertainty and discord even among the best authorities" (p. 123). In part, because of these difficulties and unsafe products the Federal Food, Drug, and Cosmetic Act in 1938 sought to minimize uncertainty about drug efficacy and safety through government oversight of development, testing, approval, and marketing of new products. This act required "new drugs to be shown safe before marketing-starting a new system of drug regulation." (About FDA, Milestones in Food and Drug Law History 1938, para. 1). Over the next 70 years thousands of drugs were proposed to the Food and Drug Administration (FDA) for approval. Once a drug is approved, then the manufacturer is required to educate prescribers about its indications, efficacy, safety, and interactions.

In order to educate prescribers about their products, pharmaceutical manufacturers have developed a breadth of strategies and tactics to communicate their messages and fulfill their obligations under the Learned Intermediary Doctrine. A few of the common methods used to inform prescribers about pharmaceutical products include:

- Face-to-face marketing via sales representatives
- Advertising in professional journals
- Publication of clinical trials data in professional journals
- Lectures/discussions by consultants

These tactics have proven very successful for pharmaceutical manufacturers. In fact, sales of prescription drugs in the U.S. in 2008 totaled more than \$291 billion (Rockoff, 2009). With so much money at stake, pharmaceutical corporations are doing everything possible to increase sales.

With the advances in drug development and increased direct-to-consumer advertising, prescribing medication for the treatment and prevention of illness and disease is at the heart of contemporary medical practice. Today, prescribers rely on pharmaceutical manufacturers for mass-produced medications that are created from complex chemical compounds, synthetic materials, biologics, and recombinant technologies. These products are developed in commercial laboratories after years of research and testing on animals and human subjects. Because of the cost and time involved in research and development of new prescription drugs, pharmaceutical companies market modern medications in a highly competitive atmosphere. In fact, global sales of generic and branded prescription drugs in 2008 were predicted to approach \$740 billion or more (Whalen, 2007, p. A12). The economic and competitive nature of the pharmaceutical industry has prompted many manufacturers to use diverse marketing and educational techniques and approaches to enlighten prescribers about their products. The dialectic between corporate profits/stakeholder expectations and required prescriber education calls into question the credibility of drug information from corporate, medical, and government sources.

Over the past decade, corporate profits and credible information appear to have been in direct conflict in a number of approved product withdrawals, but perhaps none more clearly than with Vioxx. “In patients with rheumatoid arthritis, treatment with rofecoxib (Vioxx), a selective inhibitor of cyclooxygenase-2, is associated with significantly fewer clinically important upper gastrointestinal events than treatment with naproxen, a nonselective inhibitor.” (Bombardier, Laine, Reicin, et al., 2000, p. 1520). This quote from *The New England Journal of Medicine (NEJM)* describes the benefits of a product that four years later would be pulled from the market because of cardiovascular safety concerns. The problem for the learned intermediaries who were educated about this drug from its approval in 1999 until its withdrawal from the market in 2004 is that the information they were provided by the manufacturer was often incomplete and/or biased. Five years after the Bombardier study an Editorial in *NEJM* reported, the [2000] study was designed primarily to compare gastrointestinal events in patients

with rheumatoid arthritis randomly assigned to treatment with rofecoxib (Vioxx) or naproxen (Naprosyn), but data on cardiovascular events were also monitored. Three myocardial infarctions [heart attacks], all in the rofecoxib group, were not included in the data submitted to the Journal. . . . Until the end of November 2005, we believed that these were late events that were not known to the authors in time to be included in the article published in the Journal on November 23, 2000. It now appears, however, from a memorandum dated July 5, 2000, that was obtained by subpoena in the Vioxx litigation and made available to the Journal, that at least two of the authors knew about the three additional myocardial infarctions at least two weeks before the authors submitted the first of two revisions and 4 1/2 months before publication of the article. Given this memorandum, it appears that there was ample time to include the data on these three additional infarctions in the article. The fact that these three myocardial infarctions were not included made certain calculations and conclusions in the article incorrect. (Curfman, Morrissey, and Drazen, 2005, p. 2813)

At the time of its withdrawal from the market, approximately 2 million Americans were taking Vioxx (Rubin, 2004). This misinformation is part of the “profound influence” discussed by DeAngelis and Fontanrosa (2008) and exerted by the pharmaceutical industry on prescribers’ education about prescription medications. The fact that the manufacturer and authors of the research article discussed above, and published in a prestigious professional journal, chose not to provide learned intermediaries with complete data about a product they were prescribing to millions of Americans raises the key question to be addressed in this paper.

Q: How credible is the information provided to prescribers by pharmaceutical manufacturers?

### **Credibility of Product Information**

If treatment decisions, both by prescribers and patients, rely on complete, accurate, and unbiased information about products then the credibility of the information communicated to prescribers about their drugs needs to be carefully scrutinized. Healthcare providers generally have one or two semesters of pharmacology in their professional programs. Even with 28 weeks of course work there is not enough time to explore the details of every prescription medication. In addition, the FDA approves approximately 20 new prescription products per year and frequently changes a previously approved product’s indications (Favole and Dooren, 2009). Therefore, a prescriber’s postgraduate education about new and/or older medications and various pharmaceutical options is predominantly under the direct control of the pharmaceutical industry (Ziegler, Lew, and Singer, 1995; Moynihan, 2008). Pharmaceutical manufacturers, in part to fulfill their obligation to educate learned intermediaries and in part to market and promote their products, provide numerous forums, formats, and faculty for educating prescribers

about their medications. However, before the drug maker can bring a product to market the manufacturer must gain FDA approval (Center for Drug Evaluation and Research, 2006).

The FDA was founded in the early twentieth century and its website describes the agency's mission:

The Food and Drug Administration is one of the nation's oldest and most respected consumer protection agencies.

• FDA's mission is:

- To promote and protect the public health by helping safe and effective products reach the market in a timely way
- To monitor products for continued safety after they are in use
- To help the public get the accurate, science-based information needed to improve health. (FDA, 2008, Overview, p. 1)

While these are very important goals to the health and wellness of citizens, they are equally important to the financial success of pharmaceutical corporations. This relationship between manufacturers and the FDA has been discussed by Angell and Relman (2002) who point out that “oversight. . .falls, finally, to the FDA—an agency now partially supported by the industry it regulates. That support is precarious and almost certainly conditional on the agency’s cooperation with industry” (p. 108). Numerous critics have called into question the credibility of the federal agency responsible for assuring that medical drugs and devices are safe and effective and the communication about them is accurate and unbiased. At issue is the reality that the FDA accepts millions of dollars from the industry it is charged with regulating to expedite the review of new prescription products.

Furthermore, researchers have noted that the FDA committees who review and vote on approval of new products are often comprised of industry paid consultants. Lurie, Almeida, Stine, Stine, & Wolfe (2006) reported that in nearly 75% of the more than 200 FDA meetings assessed, at least 1 member/consultant had a conflict, but less than 1 percent of those were recused. And these conflicts were for members or consultants who received in excess of \$10,000, almost a third of them received \$25,000, and nearly a quarter of the members with conflicts earned \$100,000 or more from a manufacturer. While the authors could not draw a direct relationship between the consultant’s employer/product and his/her vote on a committee, it is none-the-less a major concern from a credibility perspective. Based on such a process, how can prescribers and patients be assured that conflicts of interest and personal biases are not impacting the drug approval process at the FDA?

Fears about the FDA's process and the agency's ability to accomplish its stated mission were discussed in an *Amicus Brief* (*Wyeth v. Diana Levine*, 2008) filed by 10 present and former editors and contributing authors of the *New England Journal of Medicine*. The editors and authors argued, “. . .the FDA is in no position to ensure the safety of prescription drugs” (p. 3). The editors felt that the FDA cannot effectively evaluate the preapproval or the post-approval assessment of a drug because of the manufacturer's role in the clinical trials, approval, and safety reporting processes.

Much of this stems from the fact that the FDA is heavily dependent on the drug makers themselves for the information on which the agency bases its decisions. . . . Thus as exemplified in the cases of Pondimin/Redux, Vioxx, and Trasyolol, the drug companies have withheld key information from the FDA and ardently negotiated against stricter label warnings—all the while continuing to market their unsafe drugs to an unsuspecting public. (p. 4)

Redux, Vioxx, and Trasyolol are all products that were approved by the FDA and later found to be unsafe and eventually withdrawn from the market. These credibility concerns about the FDA contribute to the dilemma for prescribers about the veracity and science underlying the information provided to them about the safety, efficacy, and distinctions between prescription drugs. The incomplete or misinformation provided by some drug manufacturers further complicates the FDA's ability to effectively assess a drug's efficacy and safety prior to and after approval and obfuscates and/or taints the information provided to prescribers about the product. However, the FDA does not just have a problem with manufacturers' data and their consultants, FDA employees have also created credibility issues for the agency.

The FDA has been shown to have difficulty regulating itself when it comes to conflicts of interest. Cohen (2006) reports, “through an apparent loophole in agency rules, the Food and Drug Administration has allowed its employees to receive more than \$1.3 million in sponsored travel since 1999 from groups closely tied to pharmaceutical and medical device companies” (para. 1). Having staff accept money from the very industry they are regulating creates perceptions of collusion and bias for the agency. But the FDA is not the only organization that collaborates with the pharmaceutical industry and creates confusion and perpetuates deceptions. In fact, medical schools accept money for clinical trials, provide researchers, and cooperate with pharmaceutical manufacturers much to the concern of numerous critics.

The focus of medical school education should be on medical theory, science, and clinical preparation. However, complicating the process is the reach of the pharmaceutical industry.



Andreopoulos (2001) reported that medical schools rely heavily on the funding they receive from the pharmaceutical industry and in return the pharmaceutical industry relies on research performed in clinical trials by medical school faculty. According to Boyd and Bero (2000), “financial ties between academic researchers and private industry are currently under intense scrutiny. About \$1.5 billion from industry flows into academic institutions annually” (p. 2209). Perhaps even more troubling is a study by Campbell, Weismann, Ehringhaus, Rao, Moy, Feibelmann, and Goold (2007), which found more than 60% of US medical school department chairs had relationships with the pharmaceutical industry. Furthermore, for medical school faculty the possibility of promotion and fame is tied to their research ability and to publications (Jibson, 2006; Relman, 2008; Steinman, Baron, and Marlow, 2007). And the majority of their research funding comes from pharmaceutical manufacturers. It is impossible to know how these relationships with industry impact medical school administrators, faculty, and students, but clearly the risk of conflict of interest and bias impacts the credibility of their discussions and publications related to prescription drugs. But the reach of the pharmaceutical industry extends beyond medical school.

After graduation, prescribers obtain a vast amount of information regarding new therapies and evolving standards for various treatment decisions by reading professional journals. Professional associations (AMA, AOA, AANP, AAPA), as well as medical specialty organizations (Cardiology, Nephrology, Surgery, Family Practice, etc.) have at least one journal dealing with topics that are specific to a particular area of healthcare practice. These journals publish original, peer-reviewed research, case studies, book reviews, and editorials written by medical school faculty, clinical researchers, and practicing physicians, PAs, and APRNs. Providers frequently use this information to adapt their prescribing to newly emerging standards. However, some prescribers have become concerned about the views and research presented in these journal articles. Some researchers question if the information relates to objective scientific data or to pharmaceutical promotion disguised as clinical research (Wagena and Knipschild, 2005). As a result, Drazen and Curfman (2002) discuss how these concerns over conflict of interest in medical research have caused many journals to change the way in which they review and publish submissions.

In response to the exposure of several authors’/researchers’ conflicts of interest, numerous professional journals now require authors to disclose any and all financial ties with the

pharmaceutical industry before an article can be published. According to guidelines in *NEJM* (2008) “the statement should describe the authors’ relationships with companies that make products relevant to the paper. The statement should specify the type of relationships (e.g., consulting, paid speaking, grant support, equity, patents) EACH author has with EACH company” (Author Center Help, para. 1). Having financial ties with industry will not prevent an article from being published in most journals; however, *NEJM* has adopted a stricter standard than most publications when it comes to reviews and editorials. Its policy prohibits publication of reviews or editorials by authors with current, past, or planned future ties with the manufacturer of the drug being discussed. Unfortunately, even this policy is not fool proof. In 2000, *NEJM* learned it violated its own policy 19 times. In fact, “the headline in the *Boston Globe* editorial on September 1 read, ‘Malpractice at a Medical Journal’” (Kassirer, 2005, p. 53). The journal learned a stark reality, “the current system for tracking financial relationships isn’t working” (Harris, 2008, p. A1). And years after the revelations at *NEJM* Harris further revealed that,

one of the nation’s most influential psychiatrists earned more than \$2.8 million in consulting arrangements with drug makers from 2000 to 2007, [but] failed to report at least \$1.2 million of that income to his university and violated federal research rules. . . (p. A1)

The continued controversy surrounding conflict of interest in medical schools and journal articles raises further credibility issues related to the accuracy of information conveyed to learned intermediaries (Choudry, Stelfox, and Detsky, 2002). Prescribers rely on these varied publications and their authors to present the most up-to-date medical information available for treating patients. Many studies and recommendations made in professional journals have led to changes in medical practice, healthcare guidelines, and national standards of care. In addition, while providers are certainly learned in many sciences, most prescribers are not researchers or statisticians; and since the articles only present portions of the data—readers do not have all the information needed to draw their own conclusions. Kassirer (2005) notes, “one observer commented: ‘conflicts of interest are institutional weeds. They take root below the surface and become pervasive problems often long before they show their ugliness’” (p. 51). Therefore, prescribers must rely heavily on journal editors and the peer review process to ensure that the information presented in a professional journal has been thoroughly scrutinized, and represents accurate medical information on a particular topic and not hidden promotion by the

pharmaceutical industry. But conflicts of interest are just one aspect of prescribers' concerns about the credibility of the information they receive.

Beyond the conflict questions is a concern about the accuracy of the data from clinical trials. As critics have noted, the relationship between researchers and industry is perilous and fraught with many opportunities for chicanery. “. . .Merck & Co Inc, apparently manipulated dozens of publications to promote one of its products. But make no mistake—the manipulation of study results, authors, editors, and reviewers is not the sole purview of one company” (DeAngelis and Fontanarosa, 2008, p. 1833). The reality is that a large portion of pharmaceutical research is funded by the industry itself and as a consequence of that fact, the industry attempts to control the data that comes out of the various projects (Loder, 2002). Manufacturers frequently exercise their control by requiring researchers to sign confidentiality agreements that result in the researchers loss of control over the data once the project is complete. In fact, concern about this practice has caused professional journal editors to band together to oppose this restrictive process. Davidoff, DeAngelis, Drazen, Nicholls, Hoey, Højgaard, Horton, Kotzin, Nylenna, Overbeke, Sox, Van Der Weyden, and Wilkes (2001), collaborated on a statement regarding the industry's contractual policy,

as editors, we strongly oppose contractual agreements that deny investigators the right to examine the data independently or to submit a manuscript for publication without first obtaining the consent of the sponsor. Such arrangements not only erode the fabric of intellectual inquiry that has fostered so much high-quality clinical research, but also make medical journals party to potential misrepresentation, since the published manuscript may not reveal the extent to which the authors were powerless to control the conduct of a study that bears their names. (p. 786)

The overwhelming power of industry to influence the ability of researchers to publish their findings has further created uncertainty for prescribers with regards to the credibility of the drug approval and education processes.

Because the pharmaceutical industry exerts so much financial power and control over the researchers, the content of new drug applications and research articles have been called into question and now many journals rely on disclosure requirements to try and ensure unbiased authorship. But there is still great concern about the manufacturer's ability to manipulate the clinical trials and the information that is communicated about them. In fact, former *NEJM* Editor, Angell (2005) wrote in *Jurimetrics*,

I can tell you that there are many ways to design a trial to make a drug look better than it really is . . . .The fundamental problem is that drug companies have far too much control

over research on their own products—how the research is designed, how it is conducted, and how it is published. (p. 469)

This statement reiterates commonly expressed concerns regarding the lack of control investigators have over clinical trial designs and their lack of access to the raw data from the trials, or its interpretation. Pharmaceutical companies who pay for these trials want to have their own statisticians and marketing gurus review the data first and determine how to best present it for their product. However, giving in to the demands of the manufacturer still does not guarantee a researcher publication since many research results are never published because they present results that are unfavorable to the sponsoring organization. In fact, the FDA itself provides some support for this deceptive practice.

The FDA will not release all the trial results in its possession without the consent of the drug maker. Nor is the manufacturer required by the FDA to publish or otherwise publicize any of their clinical trial results. This lack of required communication of results means that many clinical trials never see the light of day. Companies, of course, are eager to publicize favorable trials, but unfavorable results remain hidden—often within the FDA, which in this regard seems to put protection of the industry’s “proprietary” interests ahead of public health. (Angell, 2005, pp. 468-469)

Therefore, like prescribers, peer reviewers only have access to the data presented in an article and that may not be all of the data from the study or studies. And it will likely not be data from a trial that did not have favorable results. However, as mentioned previously, in addition to the data dilemma, many professional journal reviewers and authors are themselves consultants and advisors to the pharmaceutical industry (DeAngelis and Fontanrosa, 2008). Kassirer (2005) a former Editor-in-Chief of *NEJM* writes,

in my experience, reviewers who are asked to excuse themselves from reviewing a manuscript because they have a financial conflict of interest rarely do. As a consequence, biased information that guides patient treatment can creep into the medical literature, and it does. (p. 85)

In addition to not recusing themselves,

reviewers may provide biased reviews that favor products of companies with which they have strong financial relationships, may fail to disclose their conflicts of interest to journal editors, or may even provide for-profit companies with confidential information obtained during the peer review process. For example, it was recently reported that a peer reviewer for the *New England Journal of Medicine* sent a confidential manuscript that he was invited to review and that demonstrated an increased mortality risk associated with rosiglitazone to

the manufacturer of this drug weeks ahead of the publication. (DeAngelis and Fontanrosa, 2008, para. 11)

However, the potential bias, unethical behaviors, and conflicts of interest do not just involve peer reviewers. Researchers/authors also contribute to the information credibility issues vis-à-vis their complicity with manufacturers.

Angell (2005) states, “one recent survey showed that authors of industry-funded studies were five times as likely to recommend the company drug as authors of studies funded by nonprofit organizations—regardless of the actual results” (p. 107). Consequently, the reality of the current situation is that prescribers, the so-called learned intermediaries, often cannot depend on conflict of interest regulations or the peer review process to remove bias and deception from the drug approval process, professional journal articles, or the information they receive about prescription drugs.

## **Discussion**

In response to the key question in this essay, bias, conflicts of interest, and manipulation of clinical trials and their data, have directly impacted the drug approval and reporting processes. Consequently, prescribers must question if the information disseminated by drug manufacturers is tainted, inaccurate, or even fallacious. This lack of credibility has a direct impact on the pharmaceutical industry’s obligation to educate learned intermediaries.

“The phrase learned intermediary was first used in *Sterling Drug, Inc. v. Cornish*” in 1966 (Clark, 2007, pp. 299-300). The Eighth Circuit Court of Appeals held that the pharmaceutical company should not be directly liable when a patient suffers an adverse effect from taking prescription medication, as long as the physician was warned of the adverse effects and contraindications associated with taking the medication. It is that notion of “warning” prescribers that is at the heart of this discussion. The rationale for the learned intermediary doctrine is based on several factors: first, the pharmaceutical company does not have a relationship with the patient; second, the pharmaceutical company has a relationship with the provider and has a duty to warn the provider of any adverse reactions or effects that the drug may have; and third, the provider who has been given adequate information regarding efficacy, dosage, administration, and side effects of a medication by the manufacturer is in the best position to decide, based on the patient’s medical history and current complaint, whether the medication should be prescribed. However, this rationale is based on courts’ assumptions that

the information communicated by the pharmaceutical companies is factual, complete, scientifically sound, and ethically communicated. Critics claims and research findings described in this study do not support those assumptions.

Pharmaceutical companies maintain that they are “obligated to do all they can to ensure that physicians, the key prescribers of prescription medicines in the health care system, are thoroughly informed about the latest medical developments” (Holmer, 2001, p. 2012). Certainly, under the current system, the industry is in the best position to provide that information since “drug companies now finance most clinical research on prescription drugs” (Angell, 2008, p. 1069). But as discussed throughout this paper, financing billions of dollars of research can lead to covert bias and/or overt deception. As Angell goes on to point out,

many publications concerning Merck’s rofecoxib [Vioxx] that were attributed primarily or solely to academic investigators were actually written by Merck employees or medical publishing companies hired by Merck. . .the company [also] manipulated the data analysis in 2 clinical trials to minimize the increased mortality associated with rofecoxib. Bias in the way industry-sponsored research is conducted and reported is not unusual and by no means limited to Merck. (p. 1069)

Based on this historical perspective, the credibility of the product information presented to prescribers must be continually called into question. Countless authors have discussed the interdependent nature of drug testing, drug approval, and drug education in this country. As this essay points out, pharmaceutical manufacturers use money and power to influence the information about its product at every stage of the process. From collaboration with medical schools and their faculty in clinical testing, to paying the FDA for expedited approval, to buying ads in professional journals and paying authors of journal articles, to using advertising and promotional tactics and sales representatives, to the financing of continuing education symposia and programs using company sponsored speakers—the information at every stage of the process is impacted directly or indirectly by the pharmaceutical manufacturer. Consequently, prescribers cannot be certain whether the communication they receive about a prescription drug is accurate, complete, and credible. This lack of credible product information is a major problem for prescribers who are expected to be learned intermediaries. But trying to assess which sources of information about prescription drugs are more credible than another creates further problems for prescribers.

Angell (2008) highlights the dichotomy for prescribers “who would be skeptical about drug company advertisements and the pitch of sales representatives [but] tend to trust the peer-

reviewed medical literature. One result of the bias in this literature is that physicians learn to practice a very drug-intense style of medicine” (p. 1071). In addition to the bias in scientific literature, it is the confusion between promotion and education that further contributes to the concerns about the accuracy of information communicated to prescribers and from prescribers to patients. This dialectical tension between health information that is accurate and clear and that which is biased or false is at the heart of the issue regarding well-informed and effective communication between “learned” prescribers and their patients.

Beyond the issue of accurate information, the financial collaborations and chicanery involved in the complicity between medical schools, faculty-researchers/presenters/authors, continuing education organizers, professional journals, the FDA and the pharmaceutical industry produce numerous ethical and health communication concerns related to these sources of product information. Consequently, based on the potential impact of financial relationships between thought-leaders/authors, healthcare organizations, and pharmaceutical companies, prescribers have no way to assess the health information they receive. Furthermore, recent problems with the publication of missing and/or inaccurate data (e.g., Vioxx, Baycol, Phenphen, and Trasyolol) and industry-sponsored thought-leaders lying about their financial ties have further contributed to prescribers’ concerns about the credibility and sources of prescription drug information (Harris, 2008).

The pharmaceutical industry tries to ignore data problems and biases and argues that they have fulfilled their legal responsibility under the learned intermediary doctrine by providing information in symposia and professional journals. However, the duty to educate prescribers has to be about more than just frequency and formats. If the source of the information communicated, the clinical trials, drug approval process and the reporting of those trials, are tainted by bias, deception, and/or unethical behavior should prescribers be held liable if the resulting data are perceived as not credible?

The issue of prescriber trust is further eroded by the fact that there is currently no third-party repository for independently obtained clinical trials data. Furthermore, communication about products generally originates from the pharmaceutical company and is distributed by consultants, publications, representatives, and organizations that have economic ties to the company that developed, tested, analyzed, and market the product.

As healthcare reform moves to center-stage in this country, the issue of pharmaceutical research, product approval, and the learned intermediary doctrine needs to be included in the discussion. It seems that the current policies allowing pharmaceutical manufacturers' money and power to dominate the process are fraught with problems. For example, it is hard to know how much of the vast prescribing of medical treatments in this country are directly related to the constant bombardment of product-specific messages to healthcare providers and patients. In addition, the role of inaccurate drug information creates its own set of additional healthcare costs and safety concerns.

Congress needs to address the ethical and legal implications of prescriber manipulation by the pharmaceutical industry. In order to prevent further harm to patients, not to mention the loss of faith in medical science as a whole, Congress needs to take action and either return the FDA to an independent agency without financial ties to the industry it regulates or find a different solution. As discussed throughout this paper, the FDA, that should be an independent, objective, assessor of drug efficacy and safety, is plagued by a lack of data control and potential bias issues. Whether the perception of bias stems from the agency's financial ties to the manufacturers it is intended to regulate, or to its policies of using reviewers with financial ties to industry, or to its lack of authority over the independence of clinical trials data—the FDA is a significant contributor to the credibility crisis in healthcare today.

If Congress cannot find a mechanism to extricate the FDA from its current co-dependent status with pharmaceutical manufacturers and consultants, then a major policy change needs to be considered. Perhaps the only way to assure independent and objective clinical trials and data reporting are to force pharmaceutical companies to pay for testing, but have no role in the product's clinical research, publication, or education efforts. All testing and reporting would be financed by the manufacturer, but administered by an independent scientific organization, like the National Institutes of Health (NIH) who currently funds and oversees some clinical trials. The NIH would independently hire researchers, recruit subjects, run the trials, analyze and publish the data, contract for continuing education and submit their findings to the FDA. The researchers and data would have no ties to the manufacturer. Of course the pharmaceutical company could still market and advertise the approved product but it would be based on independently derived clinical trials data, both positive and negative, and without the perception of FDA, researcher or thought-leader manipulation or bias.



One of the goals of such an independent process would be to eliminate the conflicts of interest that have occurred in some manufacturer controlled trials. Davidson (2007) examined 107 previously conducted clinical trials and found,

seventy-one per cent of the trials favored new therapies; 43% of these were funded by pharmaceutical firms. Of the 31 trials favoring traditional therapy, only four (13%) were supported by a pharmaceutical firm. There was a statistically significant association between the source of funding and the outcome of the study ( $p=0.002$ ). (p. 155)

From an economic perspective pharmaceutical companies do not want to pay for a clinical trial if the results are not going to benefit their products. Therefore, to try and assure the most unbiased clinical trials data possible there needs to be a truly independent, credible organization administering the trials, analyzing the data, and communicating the results.

However, until new policies can be instituted, information about pharmaceutical products will continue to have limited credibility and the sources of that information will be tainted by perceptions of bias, data manipulation, and deception. The magnitude and multitude of critical voices, combined with the health risks from inaccurate information and recalled products can no longer be ignored. Therefore, courts should re-assess the learned intermediary doctrine and its legitimacy in the face of current pharmaceutical manufacturers' practices that have included obfuscation, deceit, and inaccurate trial results. Without unbiased, ethical, and credible product information from independent sources, prescribers will continue to be potentially misinformed and unable to critically assess the data provided, educate patients, and assist them in determining the most safe and effective treatments for their illnesses or conditions. The current U.S. healthcare crisis has many etiologies, but biased and inaccurate prescribing information from manufacturers impacts millions of American lives and the legal risks of their learned intermediaries. Therefore, unless the profound influence of the pharmaceutical industry on every aspect of 21<sup>st</sup> century medicine is markedly altered or eliminated, prescribers cannot rely on the information they are provided and should not be held liable by the courts as learned intermediaries.

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