

Assessing Legal Liability in Pharmacogenetic Cases

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I. INTRODUCTION

A 1994 study disclosed that “[a]dverse drug reactions are a major cause of death in the United States.”¹ The study also disclosed that “an estimated 2 million hospitalized patients suffer from severe [adverse drug reactions] annually, even when the drugs are prescribed and administered appropriately.”² Fortunately, recent advances in genetic research are revealing why individuals vary so much in their responses to prescription drugs, and these advances are promoting the development of safer and more effective prescription drugs.³

Studies of the human genome continue to illuminate the critical roles that genes play in predisposing individuals to diseases and in producing beneficial or adverse drug reactions.⁴ Those studies show that the genetic codes of all human beings are 99.9 percent identical and that only 0.1 percent of human DNA is responsible for the individual differences in response to different prescription drugs.⁵ They reveal that individual variations in drug response are primarily caused by alternative forms of genes, called polymorphisms, which can now be detected on genetic scanners.⁶

This new genetic knowledge is rapidly transforming our understanding of health and disease.⁷ It is revolutionizing both the practice of medicine and the pharmaceutical industry.⁸ A new field of science, called pharmacogenetics, is developing which aims to produce and market prescription drugs that will be suitable for individuals with certain genotypes. Genetic tests, designed to weed out individuals who

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1. Catherine Yetter Read, *Pharmacogenomics: An Evolving Paradigm for Drug Therapy*, 11 MEDSURG NURSING 122, 123 (June 2002); see also NAT'L CTR. FOR BIOTECHNOLOGY INFO., JUST THE FACTS: A BASIC INTRODUCTION TO THE SCIENCE UNDERLYING NCBI RESOURCES, ONE SIZE DOES NOT FIT ALL: THE PROMISE OF PHARMACOGENOMICS, at <http://www.ncbi.nlm.nih.gov/About/primer/pharm.html> (last revised Feb. 13, 2003).

2. Read, *supra* note 1, at 123 (citing Jason Lazarou et al., *Incidence of Adverse Drug Reactions in Hospitalized Patients: A Meta-analysis of Prospective Studies*, 279 JAMA 1200-05 (1998)).

3. *Id.* at 122.

4. Chris Myers et al., *Genomics: Implications for Health Systems*, 17 FRONTIERS HEALTH SERVICES MGMT. 316 (2001).

5. Read, *supra* note 1, at 122.

6. *Id.*

7. NICHOLAS WADE, LIFE SCRIPT: HOW THE HUMAN GENOME DISCOVERIES WILL TRANSFORM MEDICINE AND ENHANCE YOUR HEALTH 7 (2001).

8. See *id.* at 8-9.

might have an adverse drug reaction, are being marketed along with the new gene-based drugs.⁹

The developing and marketing of new gene-based drugs and genetic tests raises complex questions about the legal liability of the manufacturers of the new drugs and tests, and about the standard of care for all health care professionals involved in prescribing and dispensing the drugs and administering the tests.¹⁰ Since misuse of personal genetic information obtained from the tests could have substantial consequences for both patients and family members, the tests need to be introduced in the context of substantial genetic counseling and guarantees of confidentiality.¹¹

During the past five years, major pharmaceutical companies have directly targeted consumers by advertising prescription drugs extensively in newspapers, magazines, and on television. In the year 2000 alone, these companies spent an estimated two billion dollars to market their products directly to consumers.¹² Their widespread overpromotion of prescription drugs, which includes the sale of drugs over the Internet, has tended to undercut the Learned Intermediary Doctrine and the fiduciary nature of the physician-patient relationship at a time when it may be more necessary than ever to preserve both.¹³

II. BASIS OF THE LEARNED INTERMEDIARY DOCTRINE

For over thirty years, the Learned Intermediary Doctrine has been a major defense available to the manufacturers of prescription drugs.¹⁴ The doctrine allows manufacturers who provide adequate instructions and warnings about the use of their prescription drugs to physicians and other relevant health care providers to escape liability for harm suffered by patients who take the drugs. It is still a viable defense in most jurisdictions, including Kansas.¹⁵

In most cases, the manufacturers of products have a duty to exercise reasonable care while directly warning consumers about any risks involved in using their products.¹⁶ However, comment k to Section 402A of the Restatement (Second) of Torts permits the manufacturers of prescription drugs (which are considered to be “unavoidably un-

9. *Id.* at 9-10.

10. Myers et al., *supra* note 4, at 13.

11. *See id.* at 14-17.

12. Jeffrey M. Drazen, *The Consumer and the Learned Intermediary in Health Care*, 346 *NEW ENG. J. MED.* 523 (2002).

13. Marcel P. Gemperli, *Rethinking the Role of the Learned Intermediary: The Effect of Direct-to-Consumer Advertising on Litigation*, 284 *MED. STUDENT JAMA* 2241 (2000).

14. Timothy A. Pratt & John F. Kuckelman, *The Learned Intermediary Doctrine and Direct-to-Consumer Advertising of Prescription Drugs*, at <http://www.thefederation.org/public/quarterly/fall00/pratt.htm> (last visited Apr. 9, 2003).

15. *See Kernke v. Menninger Clinic, Inc.*, 173 F. Supp. 2d 1117, 1121 (D. Kan. 2001).

16. Henry B. Alsobrook, Jr., *The Learned Intermediary Doctrine: Past, Present and Future*, 1994 *LEGAL MED.* 269.

safe”) to fulfill this duty by warning physicians or other health care providers who are considered learned intermediaries between the manufacturers and the patients.¹⁷

The Learned Intermediary Doctrine is based upon the premise that prescribing physicians and other involved health care providers are in the best position to correctly diagnose their patients’ medical problems and to select the appropriate drugs to prescribe based upon the following criteria: “patient sensitivity, drug efficacy, duration of treatment, potential for side effects, drug interactions with other therapy the patient may be utilizing,” as well as the patient’s own preferences in taste, mode of use, and cost.¹⁸ This doctrine recognizes that many factors, in addition to genetic predisposition, should enter into decisions about which drugs to prescribe and treatments to pursue.

III. CHALLENGES TO THE DOCTRINE

In recent years, a few exceptions to the Learned Intermediary Doctrine have been recognized in cases in which physicians do not play as active a role, such as in the administration of vaccines and oral contraceptives. The doctrine was recently codified (along with one exception to it) in Section 6(d) of the Restatement (Third) of Torts. Yet, the comments to that section left it up to the courts to determine whether the Learned Intermediary Doctrine should continue to be applied in direct-to-consumer advertising cases.¹⁹

In August 1999, the Supreme Court of New Jersey was the first court to take a stand against applying the Learned Intermediary Doctrine in a direct-to-consumer advertising case.²⁰ In *Perez v. Wyeth Laboratories, Inc.*,²¹ the court pointed out that pharmaceutical manufacturers had spent over a billion dollars in 1998 to directly influence consumers of their drugs.²² It noted that “the FDA [Food and Drug Administration] is authorized to regulate advertisements for prescription drugs [under] 21 U.S.C.A. Section 352(n) of the Food, Drug and Cosmetic Act.”²³ The court observed that modern health care providers spend much less time with patients and are much less involved in making treatment decisions under the managed health care system.²⁴

17. *Id.*

18. Michael C. Allen, *Medicine Goes Madison Avenue: An Evaluation of the Effect of Direct-to-Consumer Pharmaceutical Advertising on the Learned Intermediary Doctrine*, 20 CAMPBELL L. REV. 113, 129 (1997).

19. Pratt & Kuckelman, *supra* note 14, at 5; see RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 6(d) cmt. e (1998).

20. See Gemperli, *supra* note 13, at 2241.

21. 734 A.2d 1245 (N.J. 1999).

22. *Id.* at 1255.

23. *Id.* at 1258.

24. *Id.* at 1255; see Mitchell S. Berger, *A Tale of Six Implants: The Perez v. Wyeth Laboratories Norplant Case and the Applicability of the Learned Intermediary Doctrine to Direct-to-Consumer Drug Promotion*, 55 FOOD & DRUG L.J. 525, 534 (2000).

It emphasized that the concept of “informed consent” now requires that the patient, rather than the health care provider, play an informed role in making treatment decisions.²⁵

The New Jersey court concluded that the Learned Intermediary Doctrine should not be used as a means of relieving either drug manufacturers or health care providers of their respective duties to adequately inform and warn patients about the risks of taking prescription drugs in direct-to-consumer advertising cases.²⁶ It acknowledged that most patients want to be active participants in the treatment decision-making process, and it concluded that the patients’ interest in obtaining accurate information should prevail over any policy that protects pharmaceutical manufacturers.²⁷

The court ruled that manufacturers who directly advertise owe a duty of care to directly inform the consumers about the risks of using their products. It established a rebuttable presumption that manufacturers who comply with the FDA regulations fulfill the duty they owe to consumers of their products.²⁸ The court added that pharmaceutical manufacturers would be able to seek contribution or indemnity from health care providers who did not pass on the warnings to patients.²⁹

It is important to note that the court’s decision in *Perez* did not relieve health care providers of the duty of care that they owe as learned intermediaries to adequately inform their own patients. While emphasizing the need for patients to play a more informed role in the decision-making process, the court, in effect, highlighted the need to preserve and strengthen the fiduciary nature of the physician-patient relationship.

IV. APPLICATION OF THE LEARNED INTERMEDIARY DOCTRINE TO PHARMACOGENETICS

The increasing use of genetic tests and gene-based drugs will result in three groups of professionals (primary care physicians, geneticists, and genetic counselors) assuming greater responsibilities and incurring higher liability risks as learned intermediaries.³⁰ They will need to spend a considerable amount of time talking with, and listening to, their patients, and they should be adequately compensated for their time.³¹

25. See *Perez*, 734 A.2d at 1255.

26. *Id.* at 1262-63.

27. *Id.* at 1262; see Berger, *supra* note 24, at 535.

28. Berger, *supra* note 24, at 536.

29. *Id.*

30. Maxwell J. Mehlman, *The Human Genome Project and the Courts: Gene Therapy and Beyond*, 83 JUDICATURE 124 (1999); Interview with Dr. Kurt Wegner, Geneticist, Northside Medical Center, in Youngstown, Ohio (Nov. 17, 2002).

31. Interview with Dr. Kurt Wegner, *supra* note 30.

Primary care physicians will be expected to know enough to refer patients who might benefit from gene-based drug therapy to genetic counselors and geneticists. If they fail to properly refer patients, they may face being sued for malpractice.³² If personal financial incentives or pressures from their managed health care plan are behind their failure to properly refer patients, they can be subject to suit for both malpractice and breach of fiduciary duty.³³

Geneticists and genetic counselors will be responsible for informing patients about “the complex matrix of [the] individual genetic risk factors revealed by an expanding array of genetic tests.”³⁴ They will “help patients compare the . . . benefits and risks of” different genetic drugs and therapies.³⁵ They will also advise patients about the personal costs of submitting to genetic tests and treatment, including potential insurance and employment discrimination.³⁶ Geneticists and genetic counselors will play an essential role in preserving patients’ rights to privacy and confidentiality. Both could be sued for malpractice and breach of fiduciary duty for failure to properly fulfill their roles.

V. LIMITATIONS OF DIRECT CONSUMER MARKETING

The direct-to-consumer marketing of prescription drugs can help to educate consumers about the known genetic causes and symptoms of disease. It can encourage them to consult their own physicians and to assume a more active role in their own health care.³⁷ However, it cannot specifically address all of the individual factors that need to be taken into consideration, along with genetic factors, when deciding what medication to prescribe. Direct-to-consumer marketing cannot adequately educate the general public about the ways in which genes continuously interact with other genes, and with the environment, to promote health or illness. To attribute all illnesses solely to genetic causes would promote a false belief in genetic determinism.

Direct-to-consumer marketing is impersonal. It can never replace the important role that learned intermediaries play in evaluating what medication would be most suitable for their own patients, in obtaining their patients’ informed consent, and in preserving their patients’ confidentiality and right to privacy.

32. Mehlman, *supra* note 30, at 127.

33. *Id.*

34. *Id.* at 128.

35. *Id.*

36. *Id.*

37. Richard L. Kravitz, *Direct-to-Consumer Advertising of Prescription Drugs: Implications for the Patient-Physician Relationship*, 284 MED. STUDENT JAMA 2244, 2244-45 (2000).

VI. A NEW STANDARD OF CARE FOR GENE-BASED DRUGS AND GENETIC TESTS

In the *Perez* case, the New Jersey Supreme Court pointed out that it had previously refused to hold that all prescription drugs were “unavoidably unsafe.” It indicated that it would determine whether to apply the defect liability exception contained in comment k of Section 402A of the Restatement (Second) of Torts on a case-by-case basis.³⁸

The advent of pharmacogenetics promises to produce new prescription drugs that are not necessarily unavoidably unsafe. Using genetic tests and gene scans, manufacturers and health care providers should be able to more accurately predict in advance which individual genotypes are most likely to benefit from certain drugs and which are most likely to experience adverse drug reactions. Therefore, the standard of care they owe to patients and the determination of whether or not a prescription drug is unavoidably unsafe should be made on a case-by-case basis.

The increasing use of genetic tests should definitely give rise to a higher standard of care for the manufacturers of gene-based drugs. Genetic tests are not unavoidably unsafe like prescription drugs, and they are not regulated as stringently as drugs are regulated. Faulty test results can cause enormous physical and emotional suffering. Misuse of sensitive genetic information obtained by the tests can be personally devastating and lead to discrimination by schools, employers, and insurance companies. Therefore, companies that manufacture, distribute, and/or interpret genetic tests should not be exempt from defect liability under comment k of the Restatement (Second) of Torts.³⁹

VII. CONCLUSION

The increasing use of the new genetic technology, along with direct-to-consumer marketing, creates an urgent need for geneticists, genetic counselors, and other specialized health care providers to act as learned intermediaries and to obtain their patients’ informed consent to both genetic testing and therapy. It should place a greater burden upon manufacturers of the new gene-based drugs and genetic tests to insure that the genetic tests are highly accurate and that the new drugs are developed and marketed in ways which will adequately inform primary physicians, genetic counselors, and the general public about the benefits and risks of using them.

38. *Perez v. Wyeth Labs.*, 734 A.2d 1245, 1250 (N.J. 1999).

39. See generally Pilar N. Ossorio, *Product Liability for Predictive Genetic Tests*, 41 JURIMETRICS J. 239 (2001).