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Recommended Citation

Jennifer E. Spreng, *The Food and Drug Administration and the Pharmacy Profession: Partners to Ensure the Safety and Efficacy of Pharmacogenomic Therapy*, 13 *J. Health Care L. & Pol'y* 77 (2010).

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THE FOOD AND DRUG ADMINISTRATION AND THE PHARMACY PROFESSION: PARTNERS TO ENSURE THE SAFETY AND EFFICACY OF PHARMACOGENOMIC THERAPY

JENNIFER E. SPRENG*

INTRODUCTION

In 1998, the Food and Drug Administration (FDA) approved the drug thalidomide for the treatment of leprosy patients.¹ The decision was notable because, in response to serious birth defects in Europe associated with use of the drug,² Congress had reformed the Food, Drug, and Cosmetic Act³ in 1962 to extend the FDA's authority to use a pre-market approval process to ensure the safety and efficacy of drugs.⁴ In 1998, as a result of that pre-market approval process, the sponsor of thalidomide agreed to strategies to limit the drug's distribution through approved pharmacists pursuant to strict procedures designed to protect pregnant

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This Article is dedicated to Michael J. Aurit, who reminded me why this subject is so important.

1. Letter from Murray M. Lumpkin, Deputy Ctr. Dir., Ctr. for Drug Evaluation & Research, to Steve Thomas, Celgene Corp. (July 16, 1998), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/1998/20785ltr.pdf.

2. *See* Ctr. for the Evaluation of Risks to Human Reproduction, U.S. Dep't of Health & Human Servs., Common Concerns—Thalimodine, <http://cerhr.niehs.nih.gov/common/thalidomide.html> (last visited Feb. 20, 2010) (describing the history of the use of thalidomide and its relationship to birth defects).

3. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399 (2006).

4. Drug Amendments of 1962, Pub. L. No. 87-781, §§ 101–102, 104, 201, 76 Stat. 780, 780–82, 784–85, 792–93 (codified at 21 U.S.C. §§ 355, 374 (2006)).

women and women who might become so.⁵ The sponsor also agreed to create a register of all patients using the drug and require that all physicians and pharmacists have patients execute a specific informed consent document.⁶

Before 2007, pharmaceutical companies sometimes felt pressure from the FDA to establish special distribution systems and other post-marketing strategies on a “voluntary basis” as a condition of approving a new drug application that otherwise might not be safe.⁷ That year, Congress gave the FDA formal statutory authority to approve otherwise-unsafe drugs if a “risk evaluation and mitigation strategy . . . ensure[d] that the benefits of the drug outweigh[ed] the risks of the drug.”⁸ The FDA may now impose a risk mitigation strategy that includes allowing only “specially certified” pharmacists to dispense a drug⁹ or requiring that a drug be “dispensed to patients with evidence or other documentation of safe-use conditions, such as laboratory test results.”¹⁰

The statute goes hand-in-hand with more frequent approval and satisfactory post-marketing supervision of drugs that are safe and/or effective only for those with a specific genetic profile because the FDA can now recommend or require a

5. Margaret Gilhooley, *When Drugs Are Safe for Some but Not Others: The FDA Experience and Alternatives for Products Liability*, 36 HOUS. L. REV. 927, 943 (1999); see also Celgene Corp., Thalomid (Thalidomide) Capsules: Revised Package Insert (Jul. 15, 1998), available at <http://www.cancerconsultants.com/druginserter/Thalidomide.pdf> [hereinafter Thalidomide Package Insert] (“Under [the] restricted distribution program, only prescribers and pharmacists registered with the program are allowed to prescribe and dispense [thalidomide].”).

6. Gilhooley, *supra* note 5, at 943–44. The drug’s package insert explains these requirements and contains numerous “black box” warnings as to the serious risks of birth defects from thalidomide use, even if a woman takes only one capsule. Thalidomide Package Insert, *supra* note 5, at 1.

7. See, e.g., Tilo Mandry, *Legal Implications of Pharmacogenomics Regarding Drug Trials, Drug Labeling, and Genetic Testing for Drug Prescription: An International Approach*, 59 FOOD & DRUG L.J. 519, 532–33 (2004) (listing restrictions to assure safe use of the drug clozapine); Letter from Robert A. Sausville, Dir. of Div. of Case Mgmt., Ctr. for Biologics Evaluation & Research, to Mary Ann Lamb, Vice President of Reg. Aff., Talecris Biotherapeutics, Inc. (Jul. 6, 2009), available at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ComplianceActivities/Enforcement/UntitledLetters/ucm173449.htm> (lamenting that, because post-market reporting is voluntary, it is difficult to track adverse reactions to the drug Gamunex); Letter from Christine Hemler Smith, Regulatory Review Officer, Dep’t of Health & Human Servs., to Mark R. Szwczak, Dir. of Promotional Reg. Aff., AstraZeneca, LP (Dec. 21, 2004), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLettersToPharmaceuticalCompanies/ucm054657.pdf> (referring to AstraZeneca’s voluntary special distribution program for the drug Crestor).

8. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, sec. 901(b), § 505-1(a)(1), 121 Stat. 823, 926 (codified at 21 U.S.C.A. § 335-1 (West Supp. 2009)). Prior to this statutory authority, the FDA had taken the position that it was entitled to require manufacturers to follow strategies to mitigate potential adverse effects even when a drug was prescribed by a physician. See 21 C.F.R. §§ 208.20, .24 (2007) (providing details on the contents of medication guides that the FDA required some drug manufacturers to distribute with its drugs).

9. 21 U.S.C.A. § 355-1(f)(3)(B).

10. *Id.* § 355-1(f)(3)(D).

genetic test as part of a risk mitigation strategy.¹¹ The FDA does have less intrusive means of protecting the public.¹² For example, it can require manufacturers to include conspicuous “black box” warnings on package inserts, as well as lists of contraindications and adverse reactions in patients with specific genotypes.¹³

Black box warnings, however, like other physician-targeted approaches to ensuring drug safety, may be insufficient because physicians do not always read them.¹⁴ Similarly, both doctors and hospitals have resisted adopting technologies, such as computerized physician order entry, that would reduce medication error.¹⁵ Physicians are so engrained in the habit of prescribing drugs “off-label,” or for conditions and in doses other than those for which the FDA approved the drug, that the habit may be very difficult to break.¹⁶ Further, physicians are behind the ball in their understanding of how to use genetic information and interpret genetic tests when making prescription and dosing decisions.¹⁷ The FDA will need different risk management partners.¹⁸

11. *Id.*; see, e.g., Press Release, U.S. Food & Drug Admin., FDA Approves Updated Warfarin (Coumadin) Prescribing Information: New Genetic Information May Help Providers Improve Initial Dosing Estimates of the Anticoagulant for Individual Patients (Aug. 16, 2007), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108967.htm> (announcing approval of a labeling change for the blood-thinning drug Coumadin to explain that patients’ genetic makeup may influence their reactions to the drug, and encouraging health care providers to use genetic testing to improve their dosing of the drug).

12. See, e.g., 21 C.F.R. § 201.56–57 (2009) (allowing prescription drug box warnings that contain “contradictions” to explain situations in which the drug should not be used).

13. *Id.*

14. See, e.g., *Happel v. Wal-Mart Stores, Inc.*, 737 N.E.2d 650, 652–53 (Ill. App. Ct. 2000) (describing that the prescribing physician was unaware of the potential fatal reaction, which could have been cured by his reading the label on the drug). The learned intermediary doctrine allows manufacturers to rely on physicians to warn patients about the risks of medications, which means that as long as the warning appears on a package insert that a physician may never consult, the manufacturer may have no tort liability. Mark A. Rothstein, *Liability Issues in Pharmacogenomics*, 66 LA. L. REV. 117, 119 (2005). See generally Teresa Kelton, *Pharmacogenomics: The Re-Discovery of the Concept of Tailored Drug Therapy and Personalized Medicine*, HEALTH LAW., Jan. 2007, at 1, 5 (describing the concept of “personalized medicine,” which gives physicians more leeway in how to prescribe certain drugs to patients); Mandry, *supra* note 7, at 531–32 (describing FDA warning requirements placed on drug manufacturers).

15. Amy Jurevic Sokol & Christopher J. Molzen, *The Changing Standard of Care in Medicine: E-Health, Medical Errors, and Technology Add New Obstacles*, 23 J. LEGAL MED. 449, 467–68, 486–87 (2002) (arguing that in time, failure to embrace health technologies will harm health care providers by exposing them to potential malpractice liability, and that, while tort liability can be a useful regulatory tool, it is not the ideal first line defense against medication error).

16. See, e.g., Lars Noah, *The Coming Pharmacogenomics Revolution: Tailoring Drugs to Fit Patients’ Genetic Profiles*, 43 JURIMETRICS 1, 13–14 (2002) (noting that “the FDA has long accepted the legitimacy of off-label prescribing” as a means of personalizing medical therapy).

17. See Hong-Guang Xie & Felix W. Frueh, *Pharmacogenomics Steps Toward Personalized Medicine*, 2 PERSONALIZED MED. 325, 332 (2005) (explaining that the incorporation of pharmacogenomic testing into patient care has been slow partly due to resistance to using new technologies and methods). The full extent of “personalized medicine,” which tailors treatment according to a person’s genetic makeup, is beyond the scope of this Article. This Article is limited to

Pharmacists can help. While medical schools provide surprisingly limited training in drug therapy,¹⁹ pharmacists devote their entire professional education to the subject.²⁰ Both federal and state statutes, as well as their own professional aspirations, encourage pharmacists to participate in drug therapy decisions and counsel customers about risks, contraindications, and appropriate use of medications.²¹ Pharmacists could refuse to dispense a drug without reviewing a report of results from a simple genetic test—the “laboratory test” of the Food, Drug, and Cosmetic Act’s plain language²²—resulting in a decrease in the number of adverse reactions as well as assisting in the identification of drugs that are likely to be ineffective for that particular patient.²³ Widespread computer use in the profession would alert a pharmacist of the need to review the report and alert the physician about the potential for genetic variation in outcomes from use of the drug.²⁴ Louisiana State University Professor of Law, Science and Public Health, Michael Malinowski predicts that as innovative pharmaceuticals targeted at specific genetic profiles appear on the market, instead of “making doctors and nurses

discussing means of limiting adverse reactions to medications and identifying ineffective drugs prior to treatment.

18. See *infra* Part III.

19. See Michael J. Malinowski & Robin J.R. Blatt, *Commercialization of Genetic Testing Services: The FDA, Market Forces, and Biological Tarot Cards*, 71 TUL. L. REV. 1211, 1245 n.110 (1997) (discussing primary care providers’ lack of knowledge about genetics); Rodolfo Rodriguez et al., *Changing the Countenance of Pharmacology Courses in Medical Schools*, 18 TRENDS IN PHARMACOLOGICAL SCI. 314, 314–18 (1997) (“[I]ncreasing concern has recently been expressed about the extent to which . . . pharmacology courses provide medical students with the adequate knowledge, skills and expertise required to contend with contemporary therapeutic problems.”).

20. Gary G. Cacciatore, *Computers, OBRA 90 and the Pharmacist’s Duty to Warn*, 5 J. PHARMACY & L. 103, 103–05 (1995). Experts believe a serious limitation to the utility of genetic testing in drug prescribing is the failure of medical schools in the 1990s to provide genetics training, a problem now not easily corrected. See Malinowski & Blatt, *supra* note 19, at 1245 & n.110, 1246 (noting that in the 1990s, doctors were merely getting up to speed on genetics and were unable to keep up with patient demand on the subject, and that more education focusing on genetic technologies is needed); Gary E. Marchant, *Personalized Medicine and the Law*, ARIZ. ATT’Y, Oct. 2007, at 12, 16 (explaining that current health care professionals and institutions resist training their physicians and pharmacists in genetics testing and instead refuse to offer the tests). Pharmacists still need additional training to do this work. See Marchant, *supra*, at 16. But the comparative depth of their drug therapy training makes them more likely to get up to speed more quickly than physicians. See Cacciatore, *supra* note 20, at 104–05 (detailing the training of pharmacists).

21. See *infra* notes 44–59 and accompanying text.

22. See *supra* notes 9–10 and accompanying text.

23. See Kelton, *supra* note 14, at 3, 6 (explaining that genetic information provides health care providers with a better picture of which drugs would be effective for particular patients); Xie & Frueh, *supra* note 17, at 326, 331 (noting that genetic variations in patients may result in adverse reactions to certain drugs).

24. See Cacciatore, *supra* note 20, at 114–15 (describing the usefulness of computers to health care providers).

assume th[e] entire burden, it is likely that pharmacists and non-physician clinicians will be stepping into an expanded role in the health care process.”²⁵

This Article will argue that pharmacists are well-positioned to serve as a backstop to physicians’ prescription decisions when a particular drug is either unsafe or ineffective for a patient with a certain genetic makeup. Part I of this Article will describe recent developments in pharmacy practice that make pharmacists well-suited for that role.²⁶ Part II will discuss the FDA’s regulatory and practical authority over pharmacogenomics.²⁷ Part III will develop a legal framework to link drug approval to the practice of pharmacy,²⁸ concluding that, with respect to drugs unsuitable for patients with specific genotypes, either regulation or tort law should require that pharmacists confirm results of genetic tests prior to dispensing those drugs.²⁹

The model this Article presents will require some suspension of disbelief, at least in the short term.³⁰ The FDA regulates only a few genetic tests,³¹ and others are of questionable validity,³² which make them unreliable for dosing and dispensing decisions.³³ Testing is not currently a viable option in emergencies,³⁴

25. Michael J. Malinowski, *Law, Policy, and Market Implications of Genetic Profiling in Drug Development*, 2 HOUS. J. HEALTH L. & POL’Y 31, 55 (2002).

26. See *infra* Part I.

27. See *infra* Part II.

28. See *infra* Part III.

29. See *infra* Part III.D.

30. Malinowski, *supra* note 25, at 52 (“The day when the neighborhood pharmacist routinely tailors commercially available pharmaceuticals to account for each person’s [genetic] idiosyncrasies may be decades removed.”).

31. See, e.g., 21 C.F.R. §§ 809.3, .10, .20, .30 (2009) (regulating *in vitro* diagnostic products and analyte specific reagents); CTR. FOR DEVICES & RADIOLOGICAL HEALTH ET AL., U.S. DEP’T OF HEALTH & HUMAN SERVS., GUIDANCE FOR INDUSTRY AND FDA STAFF: PHARMACOGENETIC TESTS AND GENETIC TESTS FOR HERITABLE MARKERS 3, 5–6 (2007), available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071075.pdf> [hereinafter FDA GUIDANCE ON PHARMACOGENETIC TESTS] (describing general requirements for certain pharmacogenetic and genetic tests); CTR. FOR DEVICES & RADIOLOGICAL HEALTH & CTR. FOR BIOLOGIC EVALUATION & RESEARCH, U.S. DEP’T OF HEALTH & HUMAN SERVS., DRAFT GUIDANCE FOR INDUSTRY, CLINICAL LABORATORIES, AND FDA STAFF: IN VITRO DIAGNOSTIC MULTIVARIATE INDEX ASSAYS 3, 7 (2007), available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071455.pdf> (covering regulation of a specific type of genetic test, called *in vitro* diagnostic multivariate index assays or IVDMIAs). The terms *pharmacogenomics* and *pharmacogenetics* are not the same. Nat’l Ctr. for Biotechnology Info., One Size Does Not Fit All: The Promise of Pharmacogenomics, <http://www.ncbi.nlm.nih.gov/About/primer/pharm.html> (last visited Feb. 20, 2010). “Pharmacogenetics refers to the study of inherited differences (variation) in drug metabolism and response.” *Id.* The FDA regulates both similarly and so the Guidance applies to both types of tests. FDA GUIDANCE ON PHARMACOGENETIC TESTS, *supra*, at 1.

32. See, e.g., § 809.30(e) (requiring that reports must contain a notification that the test is not approved by the FDA).

33. See Malinowski, *supra* note 25, at 53–54 (noting that “homebrew tests” conducted by drug manufacturers escape FDA regulation, and that manufacturers often lack data to support their utility);

and often tests are prohibitively expensive.³⁵ Drugs and genetic tests may not obtain simultaneous FDA approval,³⁶ and criticism over high prices and potential antitrust violations will discourage manufacturers from “bundling” drugs and tests.³⁷ Some manufacturers are less than enthusiastic about developing drugs limited to patients with specific genetic profiles; the costs of getting a drug on pharmacy shelves make “blockbuster” drugs the preferred products in the pharmaceutical industry.³⁸ Nevertheless, several companies claim that within only a year they may have full genome sequencing services on the market³⁹—albeit for prices that in the short term only a few will be able to afford⁴⁰—which would increase the potential viability of a “small business model” of drug development and manufacture.⁴¹

Of course, the mere fact that a “solution” addresses only part of a problem is not a reason to neglect pursuing it. Point-of-sale screening can keep valuable medications such as Coumidin on the market even though they cause adverse

Mandry, *supra* note 7, at 530 (explaining that genetic testing is not the only indicator of suitability of a drug for a particular patient).

34. Mandry, *supra* note 7, at 530. This may change as complete human genome sequences become available to providers via electronic medical records, but the many complex legal and technological challenges facing both projects combine to make the possibility unlikely in the foreseeable future. See generally Keith A. Bauer, *Privacy and Confidentiality in the Age of E-Medicine*, 12 J. HEALTH CARE L. & POL'Y 47 (2009) (discussing the general privacy and confidentiality concerns associated with the growing use of electronic medical records); Kristen Rosati, *Using Electronic Health Information for Pharmacovigilance: The Promise and the Pitfalls*, J. HEALTH & LIFE SCI. L., July 2009, at 171, 182–215 (discussing privacy issues with the use of genetic testing and other health data).

35. See Wendy L. McGoodwin, *Genetic Testing in Life and Disability Insurance*, 28 THE BRIEF 24, 28 (1998) (“Because most genetic tests are quite new, they are now prohibitively expensive.”); Perry W. Payne, Jr., *Currents in Contemporary Ethics: For Asians Only? The Perils of Ancestry-Based Drug Prescribing*, 36 J. L. MED. & ETHICS 585, 585 (2008) (noting the “cost concerns” related to “genetic testing of all people”).

36. See, e.g., Marchant, *supra* note 20, at 16 (“[M]ost genetic tests currently require no regulatory approval in the United States.”).

37. Noah, *supra* note 16, at 21–22.

38. See Kelton, *supra* note 14, at 7 (explaining that advances in pharmacogenetics will likely fragment the pharmaceutical market and the blockbuster paradigm adopted by big pharmaceutical companies).

39. *Getting Personal: The Promise of Cheap Genome Sequencing*, THE ECONOMIST, Apr. 16, 2009, available at http://www.economist.com/specialreports/displaystory.cfm?STORY_ID=13437974 [hereinafter *Getting Personal*] (discussing a number of global consumer-genomics companies attempting to provide personal genetic testing, including one that expects to offer complete genome sequencing within a year); John Markoff, *I.B.M Joins Pursuit of \$1,000 Personal Genome*, N.Y. TIMES, Oct. 6, 2009, at D2, available at <http://www.nytimes.com/2009/10/06/science/06dna.html> (reporting that seventeen startup companies are preparing to offer full genome sequencing).

40. Markoff, *supra* note 39 (“Sequencing the human genome now costs \$5,000 to \$50,000 . . .”).

41. *Id.* (predicting the price of human genome sequencing will fall below \$100). It is possible that as prices decline over time, drug companies might choose to offer genome sequencing services for free in order to market personalized medications. *Getting Personal*, *supra* note 39.

reactions in patients with a specific gene mutation.⁴² A partnership between the FDA and the pharmacy profession will take advantage of current professional resources as well as provide a foundation for safe distribution of drugs in the future.⁴³

I. PHARMACY PROFESSION: YOU'VE COME A LONG WAY, BABY

The pharmacy profession has come a long way. In the early 20th century, pharmacists were still primarily compounders: professionals who prepared drugs themselves.⁴⁴ In 1951, Congress passed the Prescription Drug Amendments to the Food, Drug, and Cosmetic Act,⁴⁵ thereby separating drugs available only via prescription from those available without a prescription.⁴⁶ As a result of that legislation, pharmacists became the “gatekeeper” to the nation’s drug supply, with a monopoly over distribution of prescription drugs.⁴⁷

More recently, the pharmacy profession took another leap forward.⁴⁸ The Omnibus Budget Reconciliation Act of 1990⁴⁹ (OBRA 90) imposed several duties on pharmacists dispensing to Medicaid patients,⁵⁰ which most states adopted for all patients.⁵¹ Among its requirements were that pharmacists counsel customers about

42. See Press Release, Food & Drug Admin., FDA Clears Genetic Lab Test for Warfarin Sensitivity (Sept. 17, 2007), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108984.htm> (announcing the clearance of a test to screen for two genes that trigger sensitivity to warfarin); U.S. Office of Personnel Mgmt., Anthem Blue Cross & Blue Shield, Midwest Region: Patient Safety Initiative, <http://www.opm.gov/insure/archive/05/safety/R5.asp> (last visited Feb. 20, 2010) (explaining the point-of-sale screening process); 23andMe, Inc., Warfarin (Coumadin) Sensitivity—Genetic Testing, <https://www.23andme.com/health/Warfarin-Coumadin-Sensitivity/> (last visited Jan. 11, 2010) (discussing the impact of certain genotypes on warfarin metabolism and the potential adverse reaction if not properly administered).

43. See Jane E. Henney, Comm’r, U.S. Food & Drugs Admin., Remarks at the Conference of the National Task Force on CME Provider/Industry Collaboration: FDA Perspective on Product Promotion Issues (Sep. 24, 1999), <http://www.fda.gov/NewsEvents/Speeches/ucm054534.htm> (commenting on the increased relationship between the FDA and the pharmacy profession “to better coordinate enforcement efforts” and “to warn consumers about dangerous [sales] practices”).

44. David B. Brushwood, *The Professional Capabilities and Legal Responsibilities of Pharmacists: Should “Can” Imply “Ought”?*, 44 DRAKE L. REV. 439, 456 (1996).

45. Durham-Humphrey Drug Prescriptions Act, Pub. L. No. 82-215, 65 Stat. 648 (1951) (codified as amended at 21 U.S.C. § 353(b) (2006)); Matthew J. Seamon, *Plan B for the FDA: A Need for a Third Class of Drug Regulation in the United States Involving a “Pharmacist-Only” Class of Drugs*, 12 WM. & MARY J. WOMEN & L. 521, 539 & n.156 (2006).

46. Seamon, *supra* note 45, at 539–40.

47. William L. Allen & David B. Brushwood, *Pharmaceutically Assisted Death and the Pharmacist’s Right of Conscience*, 5 J. PHARMACY & L. 1, 2 (1995).

48. See, e.g., Steven W. Huang, *The Omnibus Reconciliation Act of 1990: Redefining Pharmacists’ Legal Responsibilities*, 24 AM. J.L. & MED. 417, 433 (1998) (noting the redefining of the pharmacists’ duties under both common law and statutory obligations).

49. Omnibus Budget Reconciliation Act of 1990, Pub. L. No. 101-508, 104 Stat. 1388.

50. Huang, *supra* note 48, at 433–34.

51. *Id.* at 434.

their medications and check for drug-therapy problems, contraindications, and similar concerns.⁵²

At approximately the same time, many of the profession's leaders began promoting a model known as "pharmaceutical care,"⁵³ a "patient-centered, outcomes-oriented, pharmacy practice" in which "pharmacists help assess therapeutic needs, prevent adverse drug reactions, develop patient-specific therapy, manage chronic disease, and monitor follow-up care."⁵⁴ The pharmaceutical care ideal envisions formal professional collaboration agreements with physicians⁵⁵ where both physicians and pharmacists are accountable for drug therapy outcomes, and pharmacists may even serve in a consultant capacity to the physician.⁵⁶

Most pharmacists remain primarily distributors of products rather than providers of services,⁵⁷ and therefore, their legal relationships with physicians and customers have been very different.⁵⁸ The longstanding common law rule was that a pharmacist could not be held liable for accurately filling a prescription apparently valid on its face.⁵⁹ The basis for the rule was the physician-patient relationship;⁶⁰ courts took the view that a pharmacist interfered with a confidential relationship if she warned a customer of potential contraindications or refused to fill a

52. *Id.*

53. Jannet M. Carmichael & Janice A. Cichowlas, *The Changing Role of Pharmacy Practice—A Clinical Perspective*, 10 ANNALS HEALTH L. 179, 180 (2001).

54. Johanna L. Keely, *Pharmacist Scope of Practice*, 136 ANNALS INTERNAL MED. 79, 80 (2002).

55. Carmichael & Cichowlas, *supra* note 53, at 180, 184, 188.

56. See David B. Brushwood, *From Confrontation to Collaboration: Collegial Accountability and the Expanding Role of Pharmacists in the Management of Chronic Pain*, 29 J.L. MED. & ETHICS 69, 78–80 (2001) (discussing accountability in collaborative drug therapy management programs, including the pharmacists' responsibility as a consultant who assists an attending physician).

57. David S. Walker & Stephen G. Hoag, *Foreword*, 44 DRAKE L. REV., at i, ii (1996).

58. See, e.g., *Eldridge v. Eli Lilly & Co.*, 485 N.E.2d 551, 554–55 (Ill. Ct. App. 1985) (stating that a pharmacist has no duty to warn a physician that the prescription is for an excessive quantity as this would cause a pharmacist to intrude upon the physician-patient relationship); David B. Brushwood, *The Pharmacist's Duty to Warn: Toward a Knowledge-Based Model of Professional Responsibility*, 40 DRAKE L. REV. 1, 11–14 (1991). Brushwood summarizes one perspective that a pharmacist is either unnecessary or downright harmful in the role of providing information or disclosing risks to patients by identifying several commonly held judicial presumptions, namely, that physicians are themselves doing a good job providing sufficient information to patients about the drugs they prescribe, that pharmacists who provide risk disclosure are second-guessing the physician, and that patients should not modify their drug use as a result of information they receive from someone other than their doctor. Brushwood, *supra*, at 12–13.

59. E.g., *Adkins v. Mong*, 425 N.W.2d 151, 152 (Mich. Ct. App. 1988) (“[A] pharmacists will not be held liable for correctly filling a prescription issued by a licensed physician.”); Brushwood, *supra* note 44, at 444 (“Until recently, courts have nearly unanimously rejected pharmacist liability for problems caused by drugs the pharmacist correctly dispensed.”).

60. E.g., *Pysz v. Henry's Drug Store*, 457 So.2d 561, 562 (Fla. Dist. Ct. App. 1984) (holding that even when the pharmacist has greater knowledge of a given drug, the physician “has the duty to know the drug that he is prescribing and to properly monitor the patient”).

prescription.⁶¹ Other courts justified not imposing a duty to warn on pharmacists with the related argument that pharmacists would not know a customer's full medical history.⁶² Judicial attitudes changed at the same time pharmacy education became more clinically oriented and sophisticated,⁶³ pharmaceutical care aspirations emerged,⁶⁴ and day-to-day practice became "computerized."⁶⁵ For example, in a case where a pharmacist filled two prescriptions for a customer written by the same doctor on two different days,⁶⁶ a Tennessee appellate court relied on state pharmacy regulations implying notions of pharmaceutical care to hold that, for the purposes of summary judgment, the pharmacist may have a duty to warn the customer of the danger of a potentially serious interaction.⁶⁷

Other states relied on notions of pharmaceutical care and the computerization of the profession when defining pharmacists' duties.⁶⁸ When overturning a summary judgment in favor of a pharmacist for failing to warn a customer when the doctor had prescribed too large a dose of medication,⁶⁹ the Missouri Court of Appeals noted that state pharmacy regulations defined a pharmacist's professional role as similar to the pharmaceutical care model:

61. *E.g.*, *McKee v. Am. Home Prods., Corp.*, 782 P.2d 1045, 1051 (Wash. 1989) ("Requiring the pharmacist to warn of potential risks associated with a drug would interject the pharmacist into the physician-patient relationship and interfere with ongoing treatment."); *Brushwood*, *supra* note 58, at 12 ("Courts also presume that a pharmacist who provides information about risk to a patient is 'second-guessing' the physician.").

62. *E.g.*, *Leesley v. West*, 518 N.E.2d 758, 762 (Ill. App. Ct. 1988) ("The foreseeability of injury to an individual consumer in the absence of any particular warning also varies greatly depending on the medical history and condition of the individual—facts [that] we cannot reasonably expect the pharmacist to know.").

63. *See Cacciatore*, *supra* note 20, at 104 (describing current requirements of pharmacy students, including learning how to communicate drug information to patients and health care providers as well as clinical rotations); *e.g.*, *Lasley v. Shrake's Country Club Pharmacy, Inc.*, 880 P.2d 1129, 1130–34 (Ariz. Ct. App. 1994). The *Lasley* court rejected the approach of courts in other jurisdictions that pharmacists have no duty to warn of possible adverse side effects or excessive doses. *Id.* at 1133–34. Instead, the court found that the defendant pharmacy owed a duty to the customer because pharmacists are professionals, and that it was up to the jury to determine whether the pharmacy's conduct breached the standard of care that the duty required. *Id.* at 1130.

64. *See supra* notes 53–56 and accompanying text.

65. *Cacciatore*, *supra* note 20, at 112–13 (noting that in one case, *Walker v. Jack Eckert Corp.*, 434 S.E.2d 63 (Ga. Ct. App. 1993), the court held that pharmacists had a duty to warn after the effective date of the OBRA 90 regulations, because patient records would be available).

66. *Dooley v. Everett*, 805 S.W.2d 380, 382 (Tenn. Ct. App. 1990).

67. *Id.* at 386.

68. *See Morgan v. Wal-Mart Stores, Inc.*, 30 S.W.3d 455, 466 (Tex. App. 2000) (noting that courts that have found an affirmative duty to warn for pharmacists on the basis of the presence of additional factors, such as known contraindications); *Hooks SuperX, Inc. v. McLaughlin*, 642 N.E.2d 514, 519 (Ind. 1994) (holding that the existence of a computerized system at the defendant pharmacy gave the pharmacist "easy access" to the customer's prescription history, a fact conducive to the finding of a duty to warn).

69. *Horner v. Spalitto*, 1 S.W.3d 519, 521–22, 524 (Mo. Ct. App. 1999).

Pharmacists have the training and skills to recognize when a prescription dose is outside a normal range. They are in the best position to contact the prescribing physician, to alert the physician about the [excessive] dose and any contraindications relating to other prescriptions the customer may be taking as identified by the pharmacy records, and to verify that the physician intended such a dose for a particular patient. We do not perceive that this type of risk management unduly interferes with the physician-patient relationship.⁷⁰

The Indiana Supreme Court also held during the 1990s that a pharmacist who filled prescriptions more quickly than indicated for a *safe use* drug had a duty to refrain from dispensing the drug further.⁷¹ That court even stated: “The relationship between pharmacist and customer is a direct one based upon contract and is independent of the relationship between physician and patient.”⁷²

A foundational case implying how the FDA might tie regulatory compliance to risk management strategies was the Illinois Supreme Court’s 2002 decision in *Happel v. Wal-Mart Stores, Inc.*⁷³ The issue on appeal was “whether a pharmacy has a duty to warn about a known drug contraindication where the pharmacy is aware of a customer’s drug allergies and knows that the medication prescribed by the customer’s physician is contraindicated for a person with those allergies.”⁷⁴ The Wal-Mart store where Heidi Happel took a prescription for Toradol kept a profile of each customer’s allergies and prescription history in its computer system.⁷⁵ The purpose of maintaining these records was to warn of contraindications.⁷⁶ The computer system would alert the pharmacist if a drug was contraindicated and then the pharmacist was supposed to telephone the physician to determine whether she should override the system and dispense the medication.⁷⁷ The pharmacist on duty the day Happel presented her prescription had no recollection of making the necessary call.⁷⁸ The court held that when the pharmacist asked customers about their allergies to various medications, Wal-Mart was “engendering reliance in the customer that the pharmacy will . . . ensure that the customer does not receive a drug to which the customer is allergic” and therefore assuming a duty to warn.⁷⁹

70. *Id.* at 523.

71. *Hooks SuperX, Inc.*, 642 N.E.2d at 516, 519.

72. *Id.* at 517.

73. 766 N.E.2d 1118 (Ill. 2002).

74. *Id.* at 1120.

75. *Id.* at 1121.

76. *Id.*

77. *Id.*

78. *Id.*

79. *Id.* at 1124–25.

As *Happel* suggests, even regulatory reform is second to computerization in changing the legal landscape of pharmacy practice.⁸⁰ Before every pharmacy had computers to maintain patient records and identify contraindications, fulfilling a duty to warn or to refuse to dispense based on a customer's prescription history was difficult.⁸¹ By 2002, however, things had changed: in *Happel*, the Wal-Mart computer system would have flashed "drug interaction" across the screen where the pharmacist could not have missed it.⁸² Lawyer and Doctor of Pharmacy, Gary G. Cacciatore explains: "Today, pharmacists rely on computers to provide comprehensive pharmaceutical care to patients . . . [including:] screening for drug-drug interactions, screening for drug-allergy interactions, screening for duplicate therapy, printing patient education materials, and maintaining patient profiles."⁸³ Legal and societal expectations for the pharmacy profession have changed enough for the FDA and physicians to partner with pharmacists to distribute drugs appropriate for a particular customer's genotype.⁸⁴

II. FDA REGULATORY AUTHORITY AND PHARMACOGENOMICS

The FDA has two frequently competing missions where innovative drugs are concerned: to ensure that drugs are "safe and effective,"⁸⁵ and also to "advanc[e] the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable"⁸⁶ These two missions translate into conservative procedures for approving new investigational and new drug

80. See Sokol & Molzen, *supra* note 15, at 463 (stating that some accreditation agencies and state governments are advocating or mandating technological solutions as a means of curbing medical prescription errors).

81. See, e.g., *Hand v. Krakowski*, 453 N.Y.S.2d 121, 122–23 (N.Y. App. Div. 1982) (holding that where a patient record identified her as an alcoholic, and a pharmacist dispensed a large amount of a psychotropic drug that is contraindicated for alcoholics, the pharmacist could be held liable for dispensing); Cacciatore, *supra* note 20, at 107 ("[T]he duty to warn recognized in *Hand* is not a general duty to warn. It has instead been limited to the unique fact situation where a pharmacist has special knowledge about the patient that created a substantial risk of serious harm.").

82. 766 N.E.2d at 1121.

83. Cacciatore, *supra* note 20, at 113.

84. See *Riff v. Morgan Pharmacy*, 508 A.2d 1247, 1251 (Pa. Super. Ct. 1986) (stating that because pharmacology is a regulated profession requiring, among other things, a specialized, accredited degree, licensing, and satisfactory performance on an exam, a pharmacist's role is not only to unthinkingly dispense medication, but also to exercise an adequate standard of care in dispensing medicine to a customer); Justina A. Molzon, *The FDA's Perspective on the Future of Pharmacy*, 44 *DRAKE L. REV.* 463, 464 (1996) (stating the FDA's position that all health-related professionals, including both pharmacists and physicians, need to work together to take advantage of technological advances so as to target information to individual patients).

85. See U.S. Food & Drug Admin., *What We Do*, <http://www.fda.gov/opacom/morechoices/mission.html> (last visited Feb. 20, 2010) ("The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of . . . drugs . . .").

86. *Id.*

applications⁸⁷ and encouragement for voluntary innovation in research and development of new drugs, devices, and biologics.⁸⁸ As a result, human genome research has produced only a few new drug applications and the industry has not taken advantage of pharmacogenomics, despite FDA cajoling.⁸⁹ The challenge now is to find ways to do so.⁹⁰

The FDA's rigorous testing requirements create a practical problem for sponsors of drugs that may require genetic testing to confirm safety: money.⁹¹ To start the process of eventual FDA approval, a sponsor must obtain an "investigational new drug" designation that allows it to conduct the required three phases of clinical tests on human beings.⁹² The first phase requires only a small number of participants—twenty to eighty—for the purpose of obtaining early evidence of safety and effectiveness.⁹³ Phase II and III studies require hundreds and thousands of participants.⁹⁴

Identifying biomarkers that will influence the safety or effectiveness of the drug for various groups can both contribute to as well as reduce these costs.⁹⁵ As early as Phase I studies, the FDA expects the sponsor to look for evidence of how subjects metabolize the drug, other biologic phenomena, and disease processes.⁹⁶ Phase I studies are the first opportunity a sponsor may have to collect data about

87. See generally *Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 697 (D.C. Cir. 2007) (upholding FDA decision not to make experimental drugs available to persons with terminal illnesses).

88. CTR. FOR DRUG EVALUATION & RESEARCH ET AL., U.S. DEP'T OF HEALTH & HUMAN SERVS., GUIDANCE FOR INDUSTRY: PHARMACOGENOMICS DATA SUBMISSIONS 7 (2005), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079849.pdf> [hereinafter PHARMACOGENETICS DATA SUBMISSIONS].

89. See U.S. FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH & HUMAN SERVS., INNOVATION OR STAGNATION: CHALLENGE AND OPPORTUNITY ON THE CRITICAL PATH TO NEW MEDICAL PRODUCTS, at i–iv (2004), available at <http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/CriticalPathInitiative/CriticalPathOpportunitiesReports/ucm113411.pdf> (noting a reduction in recent developments in the areas of drugs, devices, and biologics, summarizing various reasons for the slow technological advance and describing the FDA initiatives to stimulate development in these areas).

90. *Id.* at 5.

91. See David J. Wu, *A Pharmacogenomics Standard for FDA Drug Approval: Arbitrary and Capricious or Safe and Effective?*, 23 BIOTECHNOLOGY L. REP. 733, 737–39, 743–44 (2004) (discussing the FDA drug approval requirements and the economic challenges for the drug developer).

92. 21 C.F.R. § 312.20(a) (2009).

93. *Id.* § 312.21(a)(1).

94. *Id.* § 312.21(b)–(c).

95. STEVE OLSON ET AL., INST. OF MED., ACCELERATING THE DEVELOPMENT OF BIOMARKERS FOR DRUG SAFETY: WORKSHOP SUMMARY 1 (2009); see Stephen A. Williams et al., *A Cost-Effectiveness Approach to the Qualification and Acceptance of Biomarkers*, 5 NATURE REVIEWS DRUG DISCOVERY 897, 898 box 1, 899 (2006) (explaining that there can be situations where the costs of false results obtained by using biomarkers are greater than the value of the benefits obtained from the true results, and because it is hard to predict the efficiency of biomarkers' predictions ahead of time, some markers are not "discovered" as inefficient until after they have returned false results).

96. § 312.21(a)(2).

genetic variation in humans,⁹⁷ but unfortunately for the sponsor whose proposed drug may die on the vine based on this information, it may already have invested considerable resources to develop the drug with animal and other studies.⁹⁸ Phase II and III tests are even more onerous and expensive and have similar requirements.⁹⁹ Therefore, genetic testing even before evidence of variable outcomes emerges can control budgets.¹⁰⁰

On the other hand, the cost concern can also be a disincentive to testing drugs with genetically variable outcomes.¹⁰¹ The interface of costs and ethics is an example.¹⁰² The “common rule” applies to investigational new drug studies,¹⁰³ and therefore, an Institutional Review Board may not approve a study where the risks to some participants are not reasonable in light of the benefits.¹⁰⁴ Genetic screening can remove participants at risk from a study and target participants similar to those who will ultimately use the drug,¹⁰⁵ producing data to form a basis for ultimate FDA approval for limited population groups and indications.¹⁰⁶ The FDA has even

97. *E.g., id.* § 312.23(a)(3) (explaining that animal and other studies must be included in an investigational new drug application).

98. *See* U.S. FOOD & DRUG ADMIN., *supra* note 89, at 8 (explaining that a new medical compound entering the Phase I study process has been subject to ten years of preclinical testing but has only an eight percent chance of ultimate FDA approval, and that a ten percent improvement in predicting failures prior to clinical trials could save \$100 million per drug); Lawrence J. Lesko & Janet Woodcock, *Translation of Pharmacogenomics and Pharmacogenetics: A Regulatory Perspective*, 4 NATURE REVIEWS DRUG DISCOVERY 763, 764 (2004) (stating that developing a new drug is a massive investment that can cost upwards of \$800 million and can take an average of eight to ten years).

99. *See* § 312.21(b)–(c) (detailing the additional requirements for Phase II and III trials); U.S. FOOD & DRUG ADMIN., *supra* note 89, at 3–4 (estimating cost of bringing a new drug to market to be as high as \$0.8 to \$1.7 billion as compared to the amount needed to get to Phase I studies); Lesko & Woodcock, *supra* note 98, at 764 (noting the increasing cost and complexity of clinical trials, particularly in Phase III).

100. PETER TOLLMAN ET AL., BOSTON CONSULTING GROUP, A REVOLUTION IN R&D: HOW GENOMICS AND GENETICS ARE TRANSFORMING THE BIOPHARMACEUTICAL INDUSTRY 26–27 (2001), available at http://209.83.147.85/impact_expertise/publications/files/eng_genomicsgenetics_rep_11_01.pdf.

101. Richard Weinshilboum & Liewei Wang, *Pharmacogenomics: Bench to Bedside*, 3 NATURE REVIEWS DRUG DISCOVERY 739, 745, 747 (2004).

102. *See* Paolo Preziosi, *Science, Pharmacoeconomics and Ethics in Drug R&D: A Sustainable Future Scenario?*, 3 NATURE REVIEWS DRUG DISCOVERY 521, 524–26 (2004) (discussing the ethical and financial concerns associated with the drug development process).

103. 45 C.F.R. § 46.101 (2009); *see also* *Abney v. Amgen, Inc.*, No. 5:05-CV-254-JMH, 2005 U.S. Dist. LEXIS 14258, at *6 (E.D. Ky. July 8, 2005) (stating that 45 C.F.R. § 46.101 is “otherwise known as the Common Rule”).

104. 21 C.F.R. § 56.111(a)(2) (2009).

105. PETER TOLLMAN ET AL., *supra* note 100, at 33–34.

106. *See* 21 C.F.R. § 314.50(d)(5)(vi)(a) (requiring information about drug safety in certain populations, such as gender, age, and racial subgroups); Wu, *supra* note 91, at 738 (explaining that contemporary technology allows for genetic screening to remove patients at high risk of complications from clinical trials, rendering invalid the arguments that drug companies have used in the past to attempt to avoid FDA testing requirements). The FDA is encouraging studies with more diverse sets of

urged sponsors to submit pharmacogenomic data voluntarily by promising it will not be used against the sponsor.¹⁰⁷ While the clinical trials may be cheaper, however, the sponsor may have difficulty recouping its pre-marketing investment because of the drug's limited utility.¹⁰⁸

Studies targeted at either those with or without the relevant biomarker will not defeat approval.¹⁰⁹ To obtain approval for limited populations or indications, the sponsor must explain in the new drug application that follows the three phases of studies how the drug may or may not be both *safe*¹¹⁰ and *effective*.¹¹¹ The sponsor and the FDA must then agree on means to protect these groups at risk.¹¹² Depending on the nature and severity of the risks, these safeguards may include information on the label such as lists of contraindications, warnings, and even "black box" warnings,¹¹³ sending *Dear Doctor* letters explaining the risks of off-label use;¹¹⁴ informing pharmacists about a drug's appropriate indications and dosage;¹¹⁵ or implementing risk management strategies.¹¹⁶

Getting such a drug approved is not a simple task, but the paucity of reliable, valid genetic tests makes marketing it even more difficult.¹¹⁷ The FDA treats genetic tests as devices¹¹⁸ and has approved few, though the number and impact on

participants due to physicians' widespread "off-label" prescribing of drugs to those for whom the drugs were not tested. Noah, *supra* note 16, at 13–14.

107. CTR. FOR DRUG EVALUATION & RESEARCH ET AL., *supra* note 88, at 14.

108. Kelton, *supra* note 14, at 6–7 (explaining that pharmaceutical companies focus on "blockbuster" drugs that generate more than \$1 billion as opposed to personalized drugs).

109. *See, e.g.*, § 314.50(d)(5)(v). "Effectiveness data from other subgroups of the population of patients treated [shall be presented], when appropriate." *Id.* The submission of this information is not required for approval, and therefore a drug can be approved independent of a biomarker study.

110. *See id.* § 314.50(d)(5)(vi)(a) ("The applicant shall submit an integrated summary of all available information about the safety of the drug . . .").

111. *See id.* § 314.50(d)(5)(v) ("The applicant shall submit . . . [a]n integrated summary of the data demonstrating substantial evidence of effectiveness for the claimed indications."). The regulations refer, for example, to persons with renal failure, *id.*, but biomarkers more generally are analogous.

112. *Cf.* Michael Baram, *Making Clinical Trials Safer for Human Subjects*, 27 AM. J.L. & MED. 253, 274–75 (2001) (discussing the negotiating process between the sponsor and the FDA to determine what precautionary actions should be implemented to adequately ensure the safety of test participants); Steven E. Nissen, Editor's Commentary, *A Much-Anticipated FDA Reform Bill Is Signed into Law: Progress and Compromise*, 10 CURRENT CARDIOLOGY REP. 1, 1 (2008) (commenting on the necessary negotiation process between the pharmaceutical industry and the FDA in order to successfully relabel drugs).

113. § 201.57(a)(4), (9), (10); Mandry, *supra* note 7, at 532.

114. § 200.5; Rothstein, *supra* note 14, at 119–20.

115. § 200.7.

116. *See supra* notes 7–17 and accompanying text.

117. *See generally* Gail H. Javitt & Kathy Hudson, *The Right Prescription for Personalized Genetic Medicine*, 4 PERSONALIZED MED. 115, 115–16 (2007) (explaining that there are very few FDA-approved test kits because laboratories can develop and market their own non-FDA approved genetic test kit, which results in fewer reliable kits).

118. 21 U.S.C. § 321(h) (2006). The definition of "device" pursuant to the Food, Drug, and Cosmetic Act is:

genetic testing's availability is increasing.¹¹⁹ Most genetic tests are either *kits*¹²⁰ or a laboratory's in-house manufactured test known as a *home brew*.¹²¹ The FDA does regulate kits,¹²² but home brews are mostly unregulated.¹²³ The one home brew the FDA does regulate is the *In Vitro* Diagnostic Multivariate Index Assay (IVDMIA),¹²⁴ but the agency justifies its disputed authority with the mere thin reed of a draft guidance.¹²⁵ The FDA does require that advertising and promotional materials for home brews state that their "[a]nalytic and performance characteristics are not established" and make no other statements about the test's performance,¹²⁶

[A]n instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or . . . which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

Id. For an explanation of why a combination of the statute and the accompanying regulation may not authorize the FDA to regulate "devices" such as the *In Vitro* Diagnostic Multivariate Index Assay, see *supra* note 84.

119. See Javitt & Hudson, *supra* note 117, at 116 (noting that while the FDA has approved few test kits in the past, it has recently announced that it will begin to regulate a small subset of laboratory developed tests).

120. Gregorio M. Garcia, *The FDA and Regulation of Genetic Tests: Building Confidence and Promoting Safety*, 48 JURIMETRICS 217, 218 (2008). Kits are sold and used outside a developing laboratory or facility. *Id.*

121. Home brews are used *in-house* or in the developing laboratory. *Id.*

122. See, e.g., 21 C.F.R. § 809.30 (2009) (regulating the sale of Analyte Specific Reagents, a test developed for in-house and laboratory use).

123. 62 Fed. Reg. 62,249, 62,249 (Nov. 21, 1997) (explaining that, while the home tests are under FDA jurisdiction, the agency declines to classify them as class II or III medical devices for regulation); 61 Fed. Reg. 10,484, 10,484 (Mar. 14, 1996) (stating that "home brew" tests have not been actively regulated by the FDA); see Petition from Sean A. Johnston, Senior Vice President & General Counsel, Genentech, to Div. of Dockets Mgmt., U.S. Food & Drug Admin. (Dec. 5, 2008), available at <http://www.regulations.gov/search/Regs/home.html#documentDetail?R=09000064807d4a7e> (requesting that the FDA increase regulation of *in vitro* diagnostic tests).

124. See 21 U.S.C. § 360(e), (k) (2006) (outlining the requirements for class II and III medical devices); CTR. FOR DEVICES & RADIOLOGICAL HEALTH ET AL., U.S. DEP'T OF HEALTH & HUMAN SERVS., DRAFT GUIDANCE FOR INDUSTRY, CLINICAL LABORATORIES, AND FDA STAFF: IN VITRO DIAGNOSTIC MULTIVARIATE INDEX ARRAYS 3, 7–8 (2007) (discussing IVDMIA's and the FDA requirement of pre- and post-market approval for those that fit into class II and III); *In Vitro* Diagnostic Multivariate Index Assays; Notice of Availability, 72 Fed. Reg. 41,081, 41,081–82 (July 26, 2007) (noting that the revised draft guidance identifies IVDMIA's as a discrete category that must meet pre- and post-market device requirements); Jeffrey S. Ross et al., *Commercialized Multigene Predictors of Clinical Outcome for Breast Cancer*, 13 ONCOLOGIST 477, 485 (2008) (noting one IVDMIA that has received clearance from the FDA).

125. CTR. FOR DEVICES & RADIOLOGICAL HEALTH ET AL., *supra* note 124, at 4; Garcia, *supra* note 120, at 221. Mr. Garcia is not convinced that the FDA has authority under the Food, Drug, and Cosmetic Act to regulate IVDMIA's because the FDA has chosen to regulate the reagents used in the test devices only if they have moved in interstate commerce and not those created by the lab in which they are used. *Id.* at 227.

126. 21 C.F.R. § 809.30(d)(2), (4).

because they are “not clinically validated.”¹²⁷ The regulations also require that the laboratory put a notification on the test result that the test is not cleared or approved by the FDA.¹²⁸ Home brews are hardly the lantern on which to hang the pharmacogenomics industry.

Approved tests do provide hope that pharmacogenomics will ultimately guide physicians to appropriate drug choices for their patients.¹²⁹ Studies concluded in 2004 showed that clinical outcomes from the use of warfarin, the active ingredient in the anti-coagulant Coumadin, were associated with CYP2C9 gene variant.¹³⁰ Patients with different CYP2C9 alleles had different risks of anticoagulation, which in some patients corresponded to life-threatening bleeding.¹³¹ The FDA recently approved a test for polymorphisms in two enzymes, CYP2C9 and VKORC1, which will help determine proper dosing for patients using Coumadin.¹³² These developments could have a dramatic effect: almost ten percent of the population has the gene mutation that affects the metabolism of warfarin,¹³³ and only insulin is more often cited than Coumadin as the culprit for emergency room adverse drug events.¹³⁴

Another example is the drug Herceptin, used to treat breast cancer and the first drug approved based on pharmacogenomics.¹³⁵ The drug is indicated only if a woman is one of the thirty percent of those with breast cancer who also has an over-expression of a protein called human epidermal growth factor receptor 2 (HER2) on breast cells.¹³⁶ HER2 can make those cells multiply uncontrollably, so that women with the condition do not respond well to other breast cancer therapies.¹³⁷ Herceptin, however, can increase these women’s survival rate, and genetic tests now exist to determine if Herceptin can help.¹³⁸

127. Garcia, *supra* note 120, at 221 (quoting documents from Centers for Medicare and Medicaid Services).

128. 21 C.F.R. § 809.30(e).

129. See Xie & Frueh, *supra* note 17, at 332.

130. E.g., M. Wadelius et al., *Warfarin Sensitivity Related to CYP2C9, CYP3A5, ABCB1 (MDR1) and Other Factors*, 4 PHARMACOGENOMICS J. 40, 41 (2004); Bristol-Myers Squibb, Medication Guide: Coumadin (COU-ma-din) Tablets (Warfarin Sodium Tablets, USP) Crystalline (2009), available at http://packageinserts.bms.com/pi/pi_coumadin.pdf.

131. Wadelius et al., *supra* note 130, at 41; Bristol-Myers Squibb, *supra* note 130 (including information of risk to carriers of the CYP2C9 alleles).

132. Shashi Amur et al., *Integration and Use of Biomarkers in Drug Development, Regulation and Clinical Practice: A US Regulatory Perspective*, 2 BIOMARKERS MED. 305, 308 (2008).

133. Marchant, *supra* note 20, at 14.

134. Press Release, U.S. Food & Drug Admin., FDA Approves Updated Warfarin (Coumadin) Prescribing Information: New Genetic Information May Help Providers Improve Initial Dosing Estimates of the Anticoagulant for Individual Patients (Aug. 16, 2007), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108967.htm>.

135. Kelton, *supra* note 14, at 5.

136. *Id.*

137. *Id.*

138. *Id.*

Therefore, in the short term, FDA regulation does limit health care professionals' ability to take full advantage of pharmacogenomics, but no more than do industry leaders not developing genetically-based drugs and genetic test that provide clinically valid results. Nevertheless, society would not benefit from pharmacogenomics' full potential even if science could identify all safe and effective drugs based on a patient's genotype and technology could produce as many reliable and valid genetic tests as needed.¹³⁹ Revolutionary change is never possible without "boots on the ground."

III. PHARMACISTS: PHARMACOGENOMICS' "BOOTS ON THE GROUND"

Relying on physicians alone will not ensure that patients receive genetically compatible drugs and dosing instructions. They need a backstop:¹⁴⁰ in just one survey published in 1997, 46% of the 461 nursing home pharmacists reported that physicians regularly prescribed drugs not indicated for the elderly; that were inconsistent with labeling; and were not given according to prescriptions because of poor recordkeeping and communication with pharmacists and patients.¹⁴¹ Further, the FDA has no control over physicians' use of approved drugs, because the states, not the federal government, regulate the practice of medicine.¹⁴² Physicians are also familiar with "off-label" prescribing: prescribing drugs for purposes and in doses not listed on the FDA approved package insert;¹⁴³ personalized medicine, the

139. See Brushwood, *supra* note 44, at 459–60 (noting that achieving the full potential of pharmaceutical care is a complex interaction between physicians, patients, and pharmacists); *infra* Part III (describing how pharmacists are an integral part of reaching the full potential of pharmacogenomics).

140. See, e.g., Bob Neiner, Note, *A New Cure for Contraindication: Illinois Supreme Court Prescribes a Duty to Warn on Pharmacists: Happel v. Wal-Mart Stores, Inc.*, 766 N.E.2d 1118 (Ill. 2002), 28 S. ILL. U. L.J. 483, 490 (2004) (noting that the physician prescribed Toradol without knowing that the drug was contraindicated for an aspirin user).

141. Huang, *supra* note 48, at 419; see also Sokol & Molzen, *supra* note 15, at 462 (explaining that a physician's failure to adjust medications for patients with disease or physiological factors that alter drug action is a common form of medication error). Physicians are hardly the only culprits, however. For professionals held to a strict liability standard when its errors injure customers, it is disconcerting that pharmacists make errors when filling three to five percent of prescriptions. Eric M. Grasha, Note, *Discovering Pharmacy Error: Must Reporting, Identifying, and Analyzing Pharmacy Dispensing Errors Create Liability for Pharmacists?*, 63 OHIO ST. L.J. 1419, 1425 (2002).

142. The Sixth Circuit explains:

Absent state regulation, once a drug has been approved by the FDA, doctors may prescribe it for indications and in dosages other than those expressly approved by the FDA. This is a widely employed practice known as "off-label" use. Off-label use does not violate federal law or FDA regulations because the FDA regulates the marketing and distribution of drugs in the United States, not the practice of medicine, which is the exclusive realm of individual states.

Planned Parenthood of Cincinnati Region v. Strickland, 531 F.3d 406, 408 (6th Cir. 2008) (quoting Planned Parenthood of Cincinnati Region v. Taft, 444 F.3d 502, 505 (6th Cir. 2006)).

143. See Barbara Chevalier, *The Constitutionality of the FDA's Age-Based Plan B Regulations: Why the FDA Made the Wrong Decision*, 22 WIS. WOMEN'S L.J. 235, 249 (2007) (explaining that states retain the power to regulate both prescription and non-prescription drugs).

practical offspring of pharmacogenomics, is definitionally antithetical to off-label drug use.

Pharmacists' increased education and professional aspirations imply both greater knowledge and responsibility to assist physicians in drug therapy choices and outcomes.¹⁴⁴ A regulatory model requiring that pharmacists only fill prescriptions after receiving evidence that a customer either has a genotype appropriate for a particular drug or dose is within reach.¹⁴⁵

*A. The Model: Conditioning Dispensation on Appropriate
Genetic Test Results*

The model for ensuring that patients receive the right drugs in appropriate doses based on their genotypes requires that pharmacists condition dispensation on evidence of appropriate genetic test results.¹⁴⁶ Over the long term, applying such a model to the ideal of personalized medicine will require sophisticated genetic tests not yet available at costs that are not yet affordable,¹⁴⁷ widespread dissemination of pharmacogenomic data,¹⁴⁸ and extensive professional training.¹⁴⁹ Further, while the FDA can use its power to impose risk management strategies to require that manufacturers make sure that only "certified" pharmacists dispense drugs safe only for certain groups, this power may not extend to drugs *efficacious* only for certain groups.¹⁵⁰ Nevertheless, the FDA and the pharmaceutical industry have identified enough drugs that produce variable outcomes based on genotype and have created appropriate tests to begin implementing a program involving pharmacists that can

144. Brushwood, *supra* note 44, at 458–61.

145. See Malinowski, *supra* note 25, at 52–53 (commenting that, while individually tailored health care provided by pharmacists may be decades away, such a model is a glimpse into the foreseeable future); Gilhooley, *supra* note 5, at 945–47 (proposing similar use of distribution limits, but applying them only voluntarily). This model will only be practical, however, if regulators and the pharmaceutical industry offer products compatible with the limits of pharmacy practice.

146. See Brushwood *supra* note 44, at 459 (explaining that pharmacists would be in a position to improve health outcomes for patients by examining patient records, reports, and other information to recognize indicators of suboptimal outcomes and act on that information).

147. Kelton, *supra* note 14, at 5–6 (describing the handful of cost-effective tests and the Centers for Medicare & Medicaid Services' failure to approve and provide oversight of genetic tests); see also Malinowski, *supra* note 25, at 52–53 (noting the limitations of "homebrew" tests); Marchant, *supra* note 20, at 14–16 (noting that insurers may not see the cost-effectiveness of expensive tests).

148. See, e.g., Kelton, *supra* note 14, at 5 (explaining that package inserts fail to provide information necessary to guide pharmacogenomic therapy); Wu, *supra* note 91, at 740–41 (explaining that providing pharmacogenomic data may have to be modified on many existing drugs).

149. Xie & Frueh, *supra* note 17, at 332 (noting limited education and training of health care professionals in using pharmacogenomic data).

150. See 21 U.S.C.A. § 355-1(f)(3) (West Supp. 2009) (referring only to "[e]lements to assure *safe* use" (emphasis added)). This authorization appears on its face to apply only to drugs unsafe in certain circumstances. Efficacy is only an issue to the extent that the "benefits of the drug outweigh the risks of the drug . . ." *Id.* § 355-1(a)(1).

grow along with the FDA's exercise of its regulatory power and health care industry's ever more sophisticated knowledge over time.¹⁵¹

Such a model will only work on the ground if it is easy to use, compatible with current pharmacy practice, and enforceable via regulatory or judicial means.¹⁵² It will require using the kind of computer technology that is already standard in pharmacies to identify drugs with potential genetically-based contraindications or dosing limitations.¹⁵³ When a customer presents a prescription for such a drug, the computer software will warn the pharmacist to obtain a genetic test report or contact the physician for authority to override the warning and dispense the medication.¹⁵⁴

B. Ease of Use

The model must be easy to use. Not all pharmacists have the specialized knowledge to identify genetically-based drugs on their own,¹⁵⁵ and though professional organizations and personalized medicine advocacy groups are providing training programs,¹⁵⁶ these may take years to penetrate the entire profession.¹⁵⁷ Even if a pharmacist is "certified" according to the FDA's risk management authority,¹⁵⁸ he may not fill all prescriptions in his pharmacy,¹⁵⁹ especially in chains and managed care institutions.¹⁶⁰ In fact, most pharmacists rely heavily on low-paid pharmacy technicians who have little or no training to maximize the number of prescriptions their institution can fill.¹⁶¹ Therefore, the

151. Cf. Xie & Frueh, *supra* note 17, at 326–32 (describing numerous known drugs with genetically variable drug responses as well as speculating as to future developments related to personalized medicine).

152. See *infra* Part III.B–D.

153. See Neiner, *supra* note 140, at 491 (describing a computer system that pharmacists currently use in filling prescriptions).

154. Cf. *id.* (describing a system that displays a warning on the computer screen when a prescription is contraindicated and requires the pharmacist to override the system to continue filling the prescription).

155. See Sujit S. Sansgiry & Amit S. Kulkarni, *The Human Genome Project: Assessing Confidence in Knowledge and Training Requirements for Community Pharmacists*, 67 AM. J. PHARMACEUTICAL EDUC. 291, 295, 299 (2003) (noting that pharmacists had less than fifty percent confidence in their knowledge of pharmacogenomics).

156. Xie & Frueh, *supra* note 17, at 332.

157. Ernie Hood, *Pharmacogenomics: The Promise of Personalized Medicine*, 111 ENVTL. HEALTH PERSP. A580, A582 (2003).

158. See 21 U.S.C.A. § 355-1(f)(3)(A)–(B) (West Supp. 2009) (requiring pharmacists to become "specially certified" in order "to assure safe use").

159. See Huang, *supra* note 48, at 420 (stating that chain drug stores typically hire two or multiple pharmacists and often employ pharmacy technicians to "allow[] pharmacists to focus on counseling customers").

160. *Id.*

161. Ed Sweeney & James T. O'Donnell, *The NABP Model Act and Rules Initiative Toward Pharmacy Technicians*, in JAMES T. O'DONNELL, *DRUG INJURY: LIABILITY, ANALYSIS AND PREVENTION* 841, 842–47 (2d ed. 2005).

model must accommodate overworked professionals who have limited knowledge or difficulty keeping up with rapidly developing technology.

A computer-based identifier can help bridge the knowledge/attention gap.¹⁶² The same computer system a pharmacy uses to identify contraindications as a result of allergies or other medications can identify a drug with genetic variations in safety and efficacy.¹⁶³ All such drugs would, by definition, become “contraindications,” such that the computer system would trigger an alert every time a pharmacist enters a prescription for Coumadin, for example.¹⁶⁴ The pharmacist could only justify overriding the system and dispensing the drug if the customer provided a genetic test report showing results consistent with safe or efficacious use of the drug as prescribed, or the physician confirmed her intention to prescribe.¹⁶⁵ The evaluation of consistency would be a matter of professional discretion: one only a pharmacist could perform.¹⁶⁶

Keeping the model easy will require test facilities to standardize their result reports or present them in an easily readable format so that pharmacists working in

162. See Sokol & Molzen, *supra* note 15, at 461 (describing how technology, generally, and computers, in particular, have the ability to “simplify tasks, reduce errors, and increase efficiency”).

163. See Cacciatore, *supra* note 20, at 112–14 (describing how pharmacists rely heavily on computers to aid in decision-making such as assisting in screening for drug interactions and pharmacokinetic consults); Ioannis S. Vizirianakis, *Challenges in Current Drug Delivery from the Potential Application of Pharmacogenomics and Personalized Medicine in Clinical Practice*, 1 CURRENT DRUG DELIVERY 73, 78 (2004) (discussing the future of drug selection as evolving in a computerized environment into a “highly integrated, information-based and computer-aided pharmacotherapy based decision” that incorporates genetic information, “making drug delivery . . . more efficient and safer”).

164. See John A. Robertson et al., *Pharmacogenetic Challenges for the Health Care System*, HEALTH AFF., July–Aug. 2002, at 155, 160 (noting that in the future it is likely that the need to have a pharmacogenomic test to “determine whether a patient has a particular drug-response genotype [w]ould be listed as a contraindication, a warning, or a precaution to prescribing a drug”). This notification system would be similar not only to current pharmacy procedure, but also to less sophisticated requirements such as retail stores confirming age when consumers purchase alcoholic beverages or cigarettes. See, e.g., CTR. FOR SUBSTANCE ABUSE PREVENTION, DRAFT BEST PRACTICES FOR RESPONSIBLE RETAILING 12 (n.d.), available at http://fcpr.fsu.edu/retail/documents/BP_Report_Conference_Edition.pdf (describing checkout register computer programs that prompt the clerk to scan the customer’s identification if tobacco or alcohol are purchased); RESPONSIBLE RETAILING FORUM, RRFORUM RECOMMENDED PRACTICES FOR OFF-PREMISES ALCOHOL RETAILERS 1 (n.d.), available at http://www.rrforum.org/reports/Recommended_Practices_Off-Premises_Alcohol_Licenseses_9-09%5B1%5D.pdf (describing register computer programs that prompt cashiers to require identification and programs that read a customer’s identification electronically and calculate age).

165. Cf. *Happel v. Wal-Mart Stores, Inc.*, 766 N.E.2d 1118, 1121 (Ill. 2002) (explaining that if the pharmacy’s computer found a known contraindication a drug interaction warning would flash on the screen and could only be overridden by entering a special code after consultation with the prescribing physician).

166. See Sweeney & O’Donnell, *supra* note 161, at 844 (indicating that only pharmacists, and not technicians, “are qualified to perform tasks [that] require judgment or discretion[, and] . . . to analyze the potential for drug interactions,” and noting that pharmacists have ultimate dispensing authority).

a fast-paced environment can keep up.¹⁶⁷ The FDA lacks direct authority to impose reporting criteria on the entire genetic test market because it regulates such a small portion of available tests,¹⁶⁸ but it does have indirect tools at its disposal.¹⁶⁹

Via its risk mitigation power, the FDA can require that manufacturers supervise a program allowing “the drug [to] be dispensed to patients [only] with evidence or other documentation of safe-use conditions, such as laboratory test results.”¹⁷⁰ This power could extend to the form of the report.¹⁷¹ Physicians and hospitals can already use the Amplichip CYP450 Array, which “analyze[s] two genes . . . that encode [two] drug-metabolizing enzymes involved in the metabolism of . . . twenty-five percent of all prescription drugs;”¹⁷² the device is FDA approved and the agency could also condition ongoing approval on distribution of a standardized, simple report for a pharmacist.¹⁷³ It could do the same with approved genetic test kits.

Other departments of the federal government have played a vital role in standardizing reports.¹⁷⁴ The Centers for Medicare & Medicaid Services (CMS) has authority to ensure the validity of home brews as well as the performance of the laboratories using them,¹⁷⁵ and while the agency has not exercised that authority, CMS requires a standardized report form.¹⁷⁶ If Congress gives the FDA authority to regulate home brew tests, the FDA could then impose a standardized report form requirement on this large sector of the market.¹⁷⁷ Congress might also achieve

167. See Huang, *supra* note 48, at 419–20 (describing that pharmacists are overworked due to intense pressure to fill extreme amounts of prescriptions in very limited time periods, leading to a compromised degree of care).

168. See Garcia, *supra* note 120, at 238–39 (noting the uncertainty created by the FDA’s lack of regulation of all genetic tests); *supra* notes 118–28 and accompanying text.

169. See *infra* notes 170–78 and accompanying text.

170. 21 U.S.C.A. § 355-1(f)(3)(D) (West Supp. 2009).

171. The statute provides that the risk mitigation power may require drugs only be dispensed if there is evidence of safe-use conditions. *Id.* Because this is left as an open-ended category, it is likely that requiring a standard report form would fall under the statute. *Id.*

172. Xie & Frueh, *supra* note 17, at 331 & fig.1.

173. See, e.g., *id.* at 331; Wu, *supra* note 91, at 739–42 (describing approval, labeling, and withdrawal powers, and how the FDA uses them to obtain concessions from sponsors).

174. E.g., Bruce Patsner, *New “Home Brew” Predictive Genetic Tests Present Significant Regulatory Problems*, 9 HOUS. J. HEALTH L. & POL’Y 237, 252–53 (2009) (describing the role CMS plays in ensuring the validity of home brews).

175. See 42 C.F.R. §§ 493.1–.2, .5, .15(b)(1) (2009) (stating the conditions that all laboratories must meet to be certified to perform testing, and limiting laboratories to the performance of only certain tests of varying complexity); Patsner, *supra* note 174, at 252.

176. See § 493.1291(a), (c) (requiring a standard test report and indicating what must be included); Kelton, *supra* note 14, at 5 (noting the critics’ view that CMS “has not provided the necessary oversight”).

177. Cf. Garcia, *supra* note 120, at 224, 232–33 (explaining that the FDA provided guidance for the regulation of home brew IVDMIAs stating manufacturers must comply with medical device reporting requirements, and noting the recently proposed legislation granting FDA authority to regulate all home brew tests). One contentious issue limiting the FDA’s ability to regulate, however, would be whether

many objectives related to genetic testing if it enacted legislation similar to OBRA 90.¹⁷⁸

C. Compatibility with Current Pharmacy Practice

Another benefit of this model is its compatibility with current pharmacy practice. Using computer technology to identify contraindications is increasingly *de rigueur* in modern pharmacies.¹⁷⁹ Recently, pharmacists have begun to also control access to drugs that do not fit into the tidy prescription/over-the-counter categories.¹⁸⁰

1. Using Computers to Identify Contraindications

Virtually all pharmacists now use computers to store patient information and screen for drug interactions.¹⁸¹ These practices are not only good marketing,¹⁸² but also the common law standard of care in some jurisdictions,¹⁸³ as well as arguably a

these home brew laboratories are “practicing medicine.” *Id.* at 235. The federal government might find it attractive to reimburse laboratories for genetic testing because studies show that doing so would produce dramatic cost savings from adverse events and unproductive therapy. *See, e.g.,* Andrew McWilliam et al., *Health Care Savings from Personalizing Medicine Using Genetic Testing: The Case of Warfarin* 10–12 (AEI-Brookings Joint Ctr. for Regulatory Studies, Working Paper No. 06-23, 2006) (estimating that, if the total cost of a test plus labor to take the sample is \$350, the use of warfarin alone could result in anywhere from \$70 million to \$2.2 billion of net healthcare savings).

178. *See* Huang, *supra* note 48, at 433–34 (noting that, as enacted, OBRA 90 only applied to pharmacists who served Medicaid customers, but a majority of states extended OBRA 90 requirements to cover all prescriptions not just those reimbursable by Medicaid). Such legislation, which would require test cost reimbursement by Medicare and Medicaid, would create a strong incentive for all healthcare providers to use standardized tests to avoid the cost of two report forms. *See* Cacciatore, *supra* note 20, at 111 (describing that OBRA 90 requirements were only applicable to Medicaid patients, but most states made them applicable to all patients to prevent the creation of two standards of practice for pharmacists).

179. *See* Cacciatore, *supra* note 20, at 112 (“Computers now play a major role in almost every aspect of pharmacy practice.”); Sokol & Molzen, *supra* note 15, at 461 (noting the value computers add in the delivery of safe and effective care); *infra* Part III.C.1. Among the recommended “safe practices” in pharmacies is the use of pharmacy computers that will not dispense a drug until key health information is entered. Sokol & Molzen, *supra* note 15, at 461.

180. *See infra* Part III.C.2.

181. Cacciatore, *supra* note 20, at 112–14.

182. *See, e.g.,* Baker v. Arbor Drugs, Inc., 544 N.W.2d 727, 731 (Mich. Ct. App. 1996) (describing advertising of a pharmacy computer system designed to detect contraindications).

183. *See, e.g.,* Dooley v. Everett, 805 S.W.2d 380, 383 (Tenn. Ct. App. 1990) (quoting an expert witness who testified that in a particular Tennessee town, the standard of care required that “pharmacies maintain a patient profile system,” that it “should be reviewed by the pharmacists prior to filling a new prescription” for contraindications, and that computer technology exists to facilitate that procedure); Cacciatore, *supra* note 20, at 114–15 (quoting a prior Revco annual report explaining that Revco pharmacists, defendants in the *Dooley* case, should have relied on computers to identify contraindications).

requirement of professional codes of ethics.¹⁸⁴ Adding contraindications and warnings of potential genetic interactions with various drugs is consistent with what pharmacists already do.¹⁸⁵

Despite their advantages, computers do sometimes fail to identify contraindications,¹⁸⁶ especially when combined with user error;¹⁸⁷ therefore, such a system may be an imperfect backstop for physicians. Many pharmacies may require a substantial technology upgrade¹⁸⁸ or even additional computer training to implement this model.¹⁸⁹ Many systems allow overrides with a mere click of a function key,¹⁹⁰ and both pharmacists and pharmacy technicians are in the habit of overriding warnings and contraindications,¹⁹¹ which would make standardizing reports irrelevant. The latest systems, however, will improve safety when

184. Am. Pharm. Ass'n, *Code of Ethics for Pharmacists*, 52 AM. J. HEALTH-SYS. PHARMACY 2131, 2131, at §§ I, V (1995), available at http://www.pharmacist.com/AM/TextTemplate.cfm?Section=Practice_Resources&CONTENTID=2903&TEMPLATE=/CM/HTMLDisplay.cfm.

185. See Huang, *supra* note 48, at 434–35 (explaining that currently pharmacists must inform customers of any possible interaction with other drugs and any contraindications).

186. I. Larry Cohen et al., *Preventing Medication Errors*, in JAMES T. O'DONNELL, DRUG INJURY: LIABILITY, ANALYSIS AND PREVENTION, *supra* note 161, at 207, 217; see also Cacciatore, *supra* note 20, at 116–18 (discussing the responsibility of the pharmacist to ensure that the computer system “adequately performs those clinical functions that are considered standard in the profession”).

187. See Cacciatore, *supra* note 20, at 117–18 (describing the potential liability for pharmacists based on user error).

188. See *Over-Reliance on Pharmacy Computer Systems May Place Patients at Great Risk*, ISMP MEDICATION SAFETY ALERT! (Inst. for Safe Medication Practices, Horsham, PA), Feb. 10, 1999, available at <http://www.ismp.org/newsletters/acutecare/articles/19990210.asp> [hereinafter ISMP MEDICATION SAFETY ALERT] (stating survey results that indicate that “pharmacy computer systems need serious improvement”); Salvatore M. Barcia, *Managing Change*, HEALTH MGMT. TECH., June 2001, at 22, 22 (“Newer [pharmacy computer] systems are unquestionably superior to the [older] systems they replace.”).

189. See Barcia, *supra* note 188, at 22 (commenting on the fact that newer pharmacy computer systems that offer more clinical screenings have a higher learning curve); Bill G. Felkey & William Villaume, Commentary, *The Integration of Technology into Pharmacy Education and Practice*, INT'L J. PHARMACY EDUC., Summer 2004, at 1, 1, available at <http://www4.samford.edu/schools/pharmacy/ijpe/104/felkey.pdf> (stating that technology generally needs to be incorporated into pharmacy education).

190. See ISMP MEDICATION SAFETY ALERT, *supra* note 188 (reporting that survey “respondents’ systems require[d] no staff action (such as entering a password) to ensure that the warning was acknowledged” such that “each warning [could] be bypassed simply by pressing a function key . . .”); Patient Safety Auth., *Results of the PA-PSRS Workgroup on Pharmacy Computer System Safety*, PATIENT SAFETY ADVISORY SUPP. 2, May 31, 2007, at 1, 4 (“[A]n average of nearly [nine] in [ten] systems allow[s] . . . users to override . . . serious warnings. In most cases, the warnings could be bypassed simply by pressing a function key.”).

191. See Inst. for Safe Medication Practices, *Heed this Warning! Don't Miss Important Computer Alerts*, PHARMACY TODAY, Feb. 2009, at 52, 52 (“Pharmacists, technicians, or pharmacy interns may make a habit of bypassing certain alerts during data entry or drug use review especially if they do not realize the importance of the alert. . . . Frequent false alarms can lead to alert fatigue and complacency.”).

dispensing all drugs,¹⁹² and many pharmacists may begin adopting them for that reason alone.¹⁹³

Despite excitement about the potential of electronic medical record systems to provide universally available precision tools for filtering improvidently written prescriptions,¹⁹⁴ they will not offer practical assistance with protecting patients from genetic contraindications for decades.¹⁹⁵ Electronic medical records themselves may be commonplace by 2020,¹⁹⁶ but many more years may pass before they become *interoperable*, so that “dispersed, separately owned, and separately managed information systems” can “communicate with one another electronically to share specific bytes of data.”¹⁹⁷ Different types of health care providers—doctors, pharmacists, and hospitals, for example—also use different jargon in their records that blunt their effective use by those in other fields.¹⁹⁸ Legal and public policy concerns about privacy with respect to electronic medical records, especially as to genetic information,¹⁹⁹ may delay their use in pharmacogenomics even more.²⁰⁰ As a practical matter, routine use of interoperable electronic medical records will not be standard pharmacy practice in time to help jumpstart the personalized medicine industry.

192. *E.g.*, Sokol & Molzen, *supra* note 15, at 461.

193. *See, e.g.*, Don Dietz, Vice President, Pharmacy Healthcare Solutions Inc., Presentation at the American Society for Automation in Pharmacy Annual Technology & Issues Conference: Emerging Pharmacy Technology: Rx for Success (Jan. 27, 2006), available at http://www.asapnet.org/January2006/ASAPJan06_Presentation_Dietz.ppt (identifying “[c]ontrols and checks to minimize [prescription] errors” as a “[k]ey component[] of [n]ew [p]harmacy [d]ispensing [s]ystems”).

194. *See* Robert H. Miller & Randall R. Bovbjerg, *Efforts to Improve Patient Safety in Large, Capitated Medical Groups: Description and Conceptual Model*, 27 J. HEALTH POL. POL’Y & L. 401, 425 (2002) (describing that almost all physicians interviewed were excited about the use of future information technology to improve patient safety).

195. *See* Maren T. Scheuner et al., *Are Electronic Health Records Ready for Genomic Medicine?*, 11 GENETICS IN MED. 510, 515–17 (2009) (finding that genomics has little impact on electronic records today but may be viable in the next decade if numerous requirements are met).

196. *Cf.* Shana Campbell Jones et al., *The Interoperable Electronic Health Record: Preserving Its Promise by Recognizing and Limiting Physician Liability*, 63 FOOD & DRUG L.J. 75, 77–78 (2008). (stating that electronic medical records will reach “[eighty] percent saturation in hospitals by 2016”).

197. Rosanna M. Coffey et al., *Transforming Mental Health and Substance Abuse Data Systems in the United States*, 59 PSYCHIATRIC SERVS. 1257, 1258 (2008).

198. Jones et al., *supra* note 196, at 79.

199. 42 U.S.C.A. § 1320d-9(a) (West Supp. 2009) (stating that genetic information shall be treated as health information under the Health Insurance Portability and Accountability Act of 1996, 42 U.S.C. § 1320d(4)(B) (2006)); H.R. REP. NO. 110-28, pt. 2, at 2 (2007) (describing Congressional findings that advances in genetics give rise to “potential misuse of genetic information”); Richard Cole, *Authentic Democracy: Endowing Citizens with a Human Right in Their Genetic Information*, 33 HOFSTRA L. REV. 1241, 1256–57 (2005) (discussing state and federal legislation regarding protection of personal health information, including genetic information).

200. *See* Rosati, *supra* note 34, at 210–13 (discussing restrictions on the use of genetic testing information).

2. Increasing Pharmacist Oversight when Dispensing Drugs and Other Products

Pharmacists no longer sell only drugs classified as either prescription or over-the-counter drugs. The FDA's risk management programs authorize exceptional distribution procedures involving pharmacists.²⁰¹ A majority of pharmacists have called for a "third class" of drugs they could prescribe themselves.²⁰² Pharmaceutical care implies the existence of enhanced physician-pharmacist partnerships and collaborative relationships.²⁰³ Therefore, requiring a genetic test report prior to dispensing a drug would be within the mainstream of current and developing pharmacy practice,²⁰⁴ even if the physician retained the final say over how she treated her patient.²⁰⁵

In conjunction with physicians, pharmacists increasingly have power to authorize distribution of numerous well-known drugs.²⁰⁶ One such example is Accutane, a drug administered to treat acne, but can cause birth defects.²⁰⁷ Pharmacists are central to the *iPLEDGE* risk management program for Accutane.²⁰⁸ First, only registered pharmacists may dispense the drug.²⁰⁹ Then, because women must not purchase Accutane later than seven days from the date of the prescription, pharmacists must confirm that date.²¹⁰ Finally, every month when the woman seeks to refill her prescription, the pharmacist must contact the *iPLEDGE* program for authorization to do so.²¹¹

201. 21 U.S.C.A. § 355-1 (West Supp. 2009). See generally Deborah B. Leiderman, *Risk Management of Drug Products and the U.S. Food and Drug Administration: Evolution and Context*, 105 *DRUG & ALCOHOL DEPENDENCE* (SUPP. 1) S9, S10-12 (2009) (summarizing the role of pharmaceutical risk management in FDA drug policy).

202. Seamon, *supra* note 45, at 552.

203. See *supra* notes 53-56 and accompanying text.

204. See *supra* Part I.

205. Mandry, *supra* note 7, at 530 (noting that physicians should still exercise discretion in prescribing because "genetic testing may not enable the physician to determine that the drug is *per se* ineffective if the genetic testing shows that the patient is different from other clinical trial subjects").

206. See Brushwood, *supra* note 56, at 69 (discussing the new responsibilities of the modern pharmacist). By 2001, twenty-seven states had granted authority to pharmacists to assist physicians in collaborative drug therapy management and several additional states had proposed similar reforms. *Id.*

207. See Jeffery D. Evans & Emily W. Evans, Commentary, *Review of Eight Restricted-Access Programs and Potential Implications for Pharmacy*, 64 *AM. J. HEALTH-SYS. PHARMACY* 1302, 1306 (2007) (detailing the expanded role of the pharmacist as part of the *iPLEDGE* risk management program, which was aimed at reducing the threat of birth defects that result from use of the drug during pregnancy).

208. *Id.*

209. Ami E. Doshi, Comment, *The Cost of Clear Skin: Balancing the Social and Safety Costs of iPLEDGE with the Efficacy of Accutane (Isotretinoin)*, 37 *SETON HALL L. REV.* 625, 644 (2007).

210. *Id.* at 652. Under the *iPLEDGE* program, a woman must, among other things, have her prescription for Accutane filled within seven days of receiving it. *Id.*

211. ROCHE, ACCUTANE (ISOTRETINOIN CAPSULES) 17, 30 (2010), available at <http://www.gene.com/gene/products/information/accutane/pdf/pi.pdf>.

The FDA recently approved Plan B, an emergency contraceptive, as a *behind-the-counter* drug,²¹² again giving pharmacists an unusual role in its distribution. Plan B is unique in that it is available without a prescription to women seventeen years or older, but only by prescription to younger women.²¹³ Nevertheless, neither group may purchase the drug off the shelf.²¹⁴ The risk management strategy, CARE,²¹⁵ requires that customers request Plan B directly from the pharmacist, because the pharmacist must keep the drug “behind the counter.”²¹⁶ CARE has some provisions that may be just as onerous as requiring a genetic test report to dispense genetic-based drugs. The Plan B manufacturer must monitor compliance with the age restrictions, educate providers about the age restrictions, track how Plan B is being sold with anonymous shoppers if necessary, and report violators to State Boards of Pharmacy.²¹⁷

Congress has also weighed in on how pharmacists may sell cold medications that contain the same ingredients as the highly addictive drug methamphetamine.²¹⁸ A product such as Sudafed, which contains these ingredients,²¹⁹ must be sold from behind the counter where it must be locked away until time of purchase,²²⁰ and the seller—often a pharmacist—must deliver it directly into the purchaser’s hand,²²¹ keep a “logbook” of purchasers,²²² check each purchaser’s identification,²²³ and

212. Letter from Steven Galson, Director, Ctr. for Drug Evaluation & Research, to Joseph A. Carrado, Vice President, Clinical Reg. Aff., Duramed Research, Inc. (Aug. 24, 2006), available at http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/021045s011ltr.pdf.

213. Press Release, U.S. Food & Drug Admin., Updated FDA Action on Plan B (Levonorgestrel) Tablets (Apr. 22, 2009), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm149568.htm> (informing the public that Plan B may be marketed to women seventeen years of age or older without a prescription).

214. Memorandum from Steve Galson, Director, Ctr. for Drug Evaluation & Research on Plan B (Aug. 24, 2006), available at <http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm109782.pdf> [hereinafter Galson Memorandum].

215. See Brittany L. Grimes, Note, *The Plan B for Plan B: The New Dual Over-the-Counter and Prescription Status of Plan B and Its Impact upon Pharmacists, Consumers, and Conscience Clauses*, 41 GA. L. REV. 1395, 1415–16 (2007) (discussing the requirements of the CARE program).

216. Galson Memorandum, *supra* note 214.

217. *Id.*

218. See 21 U.S.C. § 830(d)–(e) (2006) (regulating the sale of ephedrine, pseudoephedrine, and phenylpropanolamine). These substances, common ingredients in cough medicines, can be used to manufacture methamphetamine. See Jean C. O’Connor et al., *Developing Lasting Legal Solutions to the Dual Epidemics of Methamphetamine Production and Use*, 82 N.D. L. REV. 1165, 1166, 1171 (2006) (referring to the substances in common cough medicines as “methamphetamine precursors”).

219. See Patricia Stanley, Comment, *The Combat Methamphetamine Epidemic Act: New Protection or New Intrusion?*, 39 TEX. TECH L. REV. 379, 391 (2007) (discussing a case involving the purchase of Sudafed as evidence to convict for the possession of pseudoephedrine with the intent to manufacture methamphetamine); Sudafed.com, Sudafed Nasal Decongestant Tablets, <http://www.sudafed.com/#adult/nasal/tablets> (last visited Feb. 20, 2010) (identifying pseudoephedrine as the active ingredient).

220. § 830(e)(1)(A)(i).

221. *Id.* § 830(e)(1)(A)(ii).

222. *Id.* § 830(e)(1)(A)(iii)–(iv).

limit the volume sold to any one person.²²⁴ The burden of checking genetic test reports may be relatively simple compared to the procedures necessary to sell Sudafed.²²⁵

D. Effective Means of Regulatory or Judicial Enforcement

The FDA does not have to rely solely on manufacturers to police the terms on which pharmacists dispense a drug.²²⁶ If the drug is approved for only certain uses consistent with a customer's genetic profile or is subject to a risk management strategy that relies on the pharmacist to dispense only to those customers, to do otherwise will probably be a breach of a duty of care exposing the pharmacist to common law tort liability for any damages as a result of dispensing the drug.²²⁷

The first duty would be to warn the customer of the risk of using the drug without proof of the proper genotype.²²⁸ The most recent state law warning cases holding a pharmacist liable for failure to warn were based upon whether the plaintiff reasonably relied on the pharmacist's superior knowledge and skill.²²⁹ Some hold that a pharmacy assumes the risk of liability by advertising that its services were "safe"²³⁰ or that it would check for contraindications.²³¹ Yet whether a pharmacist has a sufficient computer system may also determine whether she "knew or *should have known*" of a danger to a customer.²³² Computer systems capable of providing pharmacists with sufficient notice of gene-based contraindications may become the state of the art in the profession,²³³ and the lack of such a system could subject a pharmacist to liability on that basis alone.²³⁴

223. *Id.* § 830(e)(1)(A)(iv)(I)(aa).

224. *Id.* § 830(d)(1).

225. Compare *supra* Part III.A (discussing the model for conditioning dispensing on genetic test results), with *supra* notes 218–24 and accompanying text (discussing procedures necessary to sell Sudafed).

226. See, e.g., *Hooks SuperX, Inc. v. McLaughlin*, 642 N.E.2d 514, 517 (Ind. 1994) (recognizing that the special relationship between pharmacist and customer gives rise to a common law duty of care).

227. See *infra* notes 228–40 and accompanying text.

228. Cf. Brian L. Porto, Annotation, *Civil Liability of Pharmacists or Druggists for Failure to Warn of Potential Drug Interactions in Use of Prescription Drug*, 79 A.L.R.5th 409 (2000) (discussing federal and state cases in which the courts have determined that pharmacists must warn their customers about potential drug interactions).

229. See, e.g., *Happel v. Wal-Mart Stores, Inc.*, 766 N.E.2d 1118, 1124 (Ill. 2002) ("By asking customers about their drug allergies, the pharmacy . . . engender[ed] reliance in the customer that the pharmacy [would] . . . ensure that the customer [would] not receive a drug to which the customer is allergic.").

230. *Baker v. Arbor Drugs, Inc.*, 544 N.W.2d 727, 731 & n.1 (Mich. Ct. App. 1996) (stating that a pharmacy that advertises its use of a computer system to detect harmful drug interactions causes reliance and assumes a duty of care).

231. *Happel*, 766 N.E.2d at 1124–25.

232. *Id.* at 1123, 1125; *Baker*, 544 N.W.2d at 731.

233. Cacciatore, *supra* note 20, at 113–14; see also Helen L. Figge, *Enabling Medication Therapy Management*, 33 U.S. PHARMACIST (Sept. 18, 2008),

Common law cases also impose duties such as refusing to dispense or calling the physician where appropriate.²³⁵ Refusing to dispense when the pharmacist is on notice of a serious danger to the customer is well-recognized as a professional duty,²³⁶ and with the appropriate computer technology, the pharmacist could be considered always on notice of a genetically based contraindication every time a customer attempts to fill such a prescription.²³⁷ The standard of care would then require a pharmacist to insist on seeing a genetic test prior to dispensing the drug.²³⁸ Several courts also recognize a limited duty to call a physician to verify the physician's intent to prescribe the drug in the dose ordered, when the pharmacist should recognize it may be inappropriate.²³⁹ Doing so would allow a pharmacist to remind a physician of a genetic-based risk to a customer from the drug or the prescribed dose.²⁴⁰

The FDA might be better served by piggy-backing on the common law than it would if Congress enacted legislation, such as the Medical Device Amendments

http://www.uspharmacist.com/content/d/pharmacy_and_technology/c/10975/ (suggesting technological advances in pharmaceutical record-keeping and dispensing practices will play a critical role in the emerging field of medication therapy management).

234. See *Dooley v. Everett*, 805 S.W.2d 380, 382–83 (Tenn. Ct. App. 1990) (quoting expert testimony that the standard of care for pharmacists might include alerting patients of contraindications when technology is available to help identify drug interactions); Cacciatore, *supra* note 20, at 114–15 (noting that “[w]hile no court has held that it is malpractice per se for a pharmacist” not to have a sufficient computer system, a physician has been held liable for failing to do a sufficient literature search).

235. See, e.g., *Horner v. Spalitto*, 1 S.W.3d 519, 523 (Mo. Ct. App. 1999).

236. *Hooks SuperX, Inc. v. McLaughlin*, 642 N.E.2d 514, 516–19 (Ind. 1994) (recognizing a duty to a customer if the customer commits suicide as a result of having consumed excess amounts of a drug, where the pharmacist is on notice that the customer is consuming the drug at a much faster rate than is appropriate).

237. See *Dooley*, 805 S.W.2d at 382–85 (stating that a pharmacist has a duty to his customer to exercise the standard of care required by the pharmacy profession in the same or similar communities, which may include the use of computer technology).

238. Cf. *Hooks SuperX, Inc.*, 642 N.E.2d at 519 (“We are confident that the skilled pharmacists of our state, particularly when aided with computerized customer information records, will be readily able to determine when a prescription is being refilled at an unreasonably faster rate than the rate prescribed.”).

239. *Horner*, 1 S.W.3d at 522–24 (stating that a pharmacist's duty arises out of their unique skill set, which allows them to identify a prescription that may harm a patient, and to contact the prescribing physician to confirm or dispute a particular dose or drug). *But see Gassen v. E. Jefferson Gen. Hosp.*, 628 So.2d 256, 258–59 (La. Ct. App. 1993) (stating that a pharmacist has a duty to warn patients or notify prescribing physicians of prescriptions that could seriously harm those patients but does not have a duty to warn patients of hazardous side effects or to question a physician about the propriety of a prescription in the absence of a substantial risk of serious harm).

240. Cf. David W. Bates et al., *The Impact of Computerized Physician Order Entry on Medication Error Prevention*, 6 J. AM. MED. INFORMATICS ASS'N 313, 315 (1999) (showing that pharmacists who monitored computerized medication entry systems eliminated more than eighty percent of medication errors due to potential contraindications by alerting the prescribing physicians).

Act,²⁴¹ that would preempt state actions.²⁴² The Supreme Court has held that the Food, Drug, and Cosmetic Act²⁴³ cannot be interpreted as providing a private right of action to plaintiffs suing to recover for violations of FDA regulations,²⁴⁴ but such violations can be proof of a pharmacist's failure to fulfill her duty of care in state court.²⁴⁵

CONCLUSION

The FDA does not have to “go it alone” to protect consumers from drugs inappropriately prescribed for their genotype.²⁴⁶ Legal, practical, and aspirational developments in the pharmacy profession make pharmacists an ideal partner for achieving this goal.²⁴⁷ If the FDA and pharmacy profession work together and bring physicians into the process, in the long term the health care system and its patients will enjoy the full benefits of pharmacogenomics and personalized medicine.

241. Medical Device Amendments of 1976, Pub. L. No. 94-295, 90 Stat. 539 (codified as amended in scattered sections of 21 U.S.C.).

242. *Cf. Riegel v. Medtronic, Inc.*, 128 S. Ct. 999, 1006–07 (2008) (“[T]he [Medical Device Amendments] expressly pre-empt[] . . . state requirements different from, or in addition to, any requirement applicable . . . to the device under federal law . . .”) (internal quotations omitted).

243. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399 (2006).

244. *Merrell Dow Pharm., Inc. v. Thompson*, 478 U.S. 804, 806–07 (1986). *Merrell Dow* held that the alleged misbranding violation of the Food, Drug, and Cosmetic Act was not sufficiently “substantial” based on Congress’ failure to create a private action to grant federal question jurisdiction to the district courts. *Id.* at 814. On the other hand, it does not challenge the plaintiffs’ view that if proved, violation of the regulation would establish breach of the standard of care and causation in a products liability claim. *See id.* at 812–13 (refusing to address the question of whether a violation of the federal regulation satisfies the element of the state claim). Failure to require a genetic test report prior to dispensing a drug would be at least as, if not more, serious.

245. *Cf. Anne Erikson Haffner*, Comment, *The Increasing Necessity of the Tort System in Effective Drug Regulation in a Changing Regulatory Landscape*, 9 J. HEALTH CARE L. & POL’Y 365, 371–72 (2006) (arguing that compliance with labeling may be proof of the standard of care for physicians, but it is not a complete defense).

246. *See supra* Part III.D.

247. *See supra* Part I.

