

NEW “HOME BREW” PREDICTIVE GENETIC TESTS PRESENT SIGNIFICANT REGULATORY PROBLEMS

Bruce Patsner, M.D., J.D.*

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* Research Professor, Health Law & Policy Institute, University of Houston Law Center; B.A., Amherst College; M.D., Baylor College of Medicine; J.D., University of California-Berkeley School of Law.

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I. INTRODUCTION

The past decade has witnessed a revolution in terms of medical products (pharmaceuticals, devices, and biologics) that offer predictive medical services, such as cancer drug selection and individual genetic testing never before available to the American public. Some of these new products are reaching U.S. markets via the traditional route of FDA evaluation of safety and efficacy prior to marketing; however, the majority of these products readily circumvent many FDA rules and regulations, or even FDA jurisdiction entirely. Even new predictive or preventive products that the FDA evaluates for efficacy and safety may raise serious issues about how efficacy is measured or whether the long-term safety risks can ever really be known prior to approval. Yet, what has been even more dramatic is the commercialization of new predictive genetic testing completely outside the supervision of healthcare professionals and an apparent paucity of regulatory oversight over the quality and accuracy of such testing.

This article explores some of the regulatory and public health concerns surrounding this new generation of predictive medical

products, particularly individual genetic testing. These tests are classified as medical devices under the 1938 Federal Food, Drug and Cosmetic Act (FDCA Stat.). However, the diagnostic testing industry is not regulated uniformly by the federal government and is almost exclusively a function of whether the predictive medical device is categorized as a “home brew” diagnostic test. The lack of direct FDA control over this industry creates a public health and safety “regulatory black hole.”

This article makes two major regulatory points. First, the importance of the FDA as a regulatory force has been offset by the ubiquities of “home brew” predictive medical tests, particularly personalized genetic testing, which essentially function outside the penumbra of FDA oversight, to some degree. The second major point is that neither the states nor the medical profession is likely to fill this regulatory niche adequately. Two of the most recent developments in predictive genetic medical technology help illustrate this latter point. The article concludes by advancing several solutions to these regulatory concerns.

II. THE WIDE SPECTRUM OF NEW OF PREDICTIVE MEDICAL PRODUCTS

The past decade has witnessed the availability of a dazzling array of innovative new medical products, which may be categorized under the newly-coined term “personalized medicine.”¹ Recent advances in new medical disciplines such as proteonomics,² pharmacogenomics,³ and bioinformatics⁴ have generated biological

¹ Jeffrey N. Gibbs, *Personalized Medicine: Panacea or Pipedream?*, UPDATE, Sept.-Oct. 2008 FOOD AND DRUG LAW INSTITUTE 6, 6. The author correctly points out that the term “personalized medicine” is not self-defining but generally revolves around tailoring of individual therapies and diagnostics “to meet the specific needs of each patient.” *Id.* The true potential of such technology probably lies somewhere between the hyped ability to revolutionize healthcare and the notion that its benefits will not yield significant results for many years. *See id.*

² Lance A. Liotta et al., *Clinical Proteonomics. Personalized Molecular Medicine*, 286 JAMA 2211 (2001).

³ Kathryn A. Phillips et al., *Potential Role of Pharmacogenomics in Reducing Adverse Drug Reactions, A Systematic Review*, 286 JAMA 2270 (2001).

or genetic tests that, for example, allow oncologists to predict which women with breast cancer are more likely to have a favorable response to the drug Herceptin or other cancer drugs,⁵ predict which “low risk” breast cancer patients are more likely to develop metastatic disease,⁶ or predict the risk of developing ovarian or breast cancer based on family history and ethnic background.⁷ Additional predictive diagnostic testing allows internists to tailor drug therapy for individual patients with HIV or other chronic diseases⁸ to minimize adverse events as well as to select proper doses of certain drugs.

Less conventional predictive genetic testing that was recently marketed includes a wide array of “home brew” genetic tests. These tests have enjoyed recent media exposure through direct-to-consumer marketing, which advertises the availability and purported ability of such testing to predict the likelihood of an individual developing any one of a number of medical, as well as non-medical, personality traits.⁹ It is now possible for individuals to obtain information about their genetic susceptibility to dozens of common

⁴ Robert M. Caltih & Geoffrey S. Ginsburg, *Organizational Improvements to Enhance Modern Clinical Epidemiology*, 300 JAMA 2300 (No. 19, 2008); see also Michael M. Shi et al., *Pharmacogenetic Application in Drug Development and Clinical Trials*, 29 DRUG METABOLISM AND DISPOSITION 591 (2001) (discussing the impact of pharmacogenetics on drug development and the potential impact on the practice of medicine).

⁵ Wei Peng Yong & Federico Innocenti, *Translation of Pharmacogenetic Knowledge Into Cancer Therapeutics*, 5(9) CLINICAL ADVANCES IN HEMATOLOGY AND ONCOLOGY 698 (2007).

⁶ Andrew Pollack, *Test to Predict Breast Cancer Relapse Is Approved*, N.Y. TIMES, Feb. 7, 2007 at A1.

⁷ See, e.g., The American College of Obstetricians and Gynecologists, ACOG COMMITTEE OPINION ON TECHNOLOGY ASSESSMENT IN OBSTETRICS AND GYNECOLOGY, *Genetics and Molecular Diagnostic Testing*, Number 1, July 2002. (“For example, 85% of women with a BRCA1 mutation develop breast cancer during their lifetime; therefore, the finding of a BRCA1 mutation indicates a strong predisposition to breast cancer, but it does not indicate which women with the mutation will develop a malignancy. Therefore, it may only be possible to provide patients with a description of the natural history of the disorder and an estimate of the frequency of specific features in patients with similar mutations.”).

⁸ C. Roland Wolf et al., *Science, Medicine, and the Future Pharmacogenetics*, 320 BR. MED. J. 987 (2000).

⁹ Amy Harmon, *My Genome, Myself: Seeking Clues in DNA*, N.Y. TIMES, Nov. 17, 2007 at A1, available at <http://www.nytimes.com/2007/11/17/us/17dna.htm?pagewanted=print> (last visited October 22, 2008).

and/or complex disorders, as well as information about the pharmaco-therapeutics of the medications they are taking, without the direct involvement of the medical profession or oversight by federal agencies, primarily the United States Food and Drug Administration (FDA).¹⁰ Some of these new predictive genetic tests are being promoted directly to consumers by individual laboratories, commercial manufacturers, or academic medical centers with little substantive information about the validity and clinical utility of the information they are providing.

Virtually all of these new predictive medical products, especially genetic tests, are classified as medical devices under the 1938 Federal Food, Drug and Cosmetic Act (FDCA).¹¹ The original definition of a medical device was provided in the Act and, though modified over the years, has preserved the key distinction between drugs and devices; the former work through chemical action or by being metabolized, while the latter do not.¹² The classification of a medical product as a medical device, as opposed to as a drug or biologic, is of critical importance because the manner in which such products are evaluated, approved, and marketed differs enormously.

FDA's stated mission is to protect the health of the U.S. public and to ensure that marketed medical products such as prescription drugs, medical devices including predictive diagnostic genetic tests, and biologics such as vaccines are safe, effective, and have sufficient controls over manufacturing quality and reproducibility of data such that consumers can be assured that the healthcare information they

¹⁰ *Id.*

¹¹ FEDERAL FOOD, DRUG AND COSMETIC ACT, 21 U.S.C. §§ 301 ET SEQ (1938) [hereinafter FDCA] (originally enacted as Act of June 25, 1938 Ch. 675 § 201, 52 Stat 1040 (1938)).

¹² FDCA, 21 U.S.C. § 321(h) (The term "device"...means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is...(2) 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 (3) which is intended to affect the structure or any function of the body of man or other animals, and 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).

are receiving is valid and beneficial.¹³ Although the new medical product approval system has not proved to be without serious faults of late, particularly in the area of drug safety and post-marketing surveillance,¹⁴ the current regulatory system has for the most part done an admirable job of assuring baseline manufacturing consistency, quality of information, efficacy, and safety for most of the new products it approves.¹⁵ The regulatory challenge the FDA faces for new predictive drug and personal genetic information testing is less whether it can rise to the occasion and effectively evaluate such technologies than whether it will be the major player in the regulation of such medical products.

III. ESTABLISHING EFFICACY AND SAFETY FOR PREDICTIVE MEDICAL PRODUCTS

A review of basic FDA new medical product evaluation and approval is necessary in order to appreciate the regulatory dilemma new predictive medical products such as genetic testing present for public health and safety. The traditional method for new prescription medical products to reach the U.S. markets is through the United States Food and Drug Administration (FDA) which formally evaluates the product for efficacy, safety, and consistent, good manufacturing quality.¹⁶ Although the details of new drug,

¹³ FDA, MISSION STATEMENT, available at <http://www.fda.gov/opacom/morechoices/mission.html> (last visited Jan. 19, 2009) (“The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation’s food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.”).

¹⁴ MARCIA ANGELL, THE TRUTH ABOUT THE DRUG COMPANIES. HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT (2004); see also Barbara J. Evans & David A. Flockhart, *The Unfinished Business of U.S. Drug Safety Regulation*, 61 FOOD & DRUG L.J. 45 (2006).

¹⁵ Howard Markel, *Why America Needs a Strong FDA*, 294 JAMA 2489 (2005).

¹⁶ See PETER BARTON HUTT et al., FOOD AND DRUG LAW. CASES AND MATERIALS (3rd ed. 2007) [hereinafter Hutt Casebook], for a comprehensive description of how the FDA approves all new types of products.

biological, and medical device evaluation and approval are beyond the scope of this article, a brief description of the critical similarities and differences is necessary to better understand the regulatory problems some of these new medical technologies present. Most importantly, the rules and regulations for FDA approval of a new medical product apply only to those products which FDA has jurisdiction over.

New prescription drug and new biological (e.g., vaccine) medical products are evaluated by different centers at FDA (the Center for Drug Evaluation and Research [CDER] and the Center for Biologics Evaluation and Research [CBER], respectively) but the basic manner in which new products are approved are similar. The FDA center with primary jurisdiction will review the product and give it one approval;¹⁷ the primary jurisdiction is based on the primary mode of action of the product.¹⁸ Sponsors submit either a new drug application (NDA) or biologics licensing application (BLA) to the respective division (e.g., oncology, cardio-renal, reproductive) within the appropriate center at the agency. These new marketing applications generally must contain extensive chemistry, pharmacology, manufacturing, and clinical trial data, which is evaluated by the FDA to determine if the product is safe and effective, as well as whether it demonstrates good manufacturing practices (GMPs).¹⁹ Although the endpoints for determining whether a new drug or biologic “works” vary greatly depending on the product, division, and even individual medical reviewer, as a rule the clinical endpoints and statistical criteria which a sponsor must prove in clinical testing are agreed to between FDA and the sponsor during phase II testing prior to undertaking the large, expensive clinical trial needed for marketing approval. These efficacy endpoints are generally contained in a statistical analysis plan (SAP), which is part of the NDA or BLA package. Generally, two large randomized

¹⁷ 21 C.F.R. § 5.33 (2003).

¹⁸ *Id.* See ALSO SAFE MEDICAL DEVICE ACT, PUB. L. 101-629, 104 STAT. 4511 (1990).

¹⁹ MARK MATHIEU, *NEW DRUG DEVELOPMENT: A REGULATORY OVERVIEW* (6th ed. 2002) [hereinafter Mathieu]. Excellent information on the approval process can also be found readily on both CDER and CBER websites respectively, available at www.cder.fda.gov and www.cber.fda.gov.

controlled clinical trials are required in order to approve a new drug or biological.²⁰ Routes do exist to allow drugs or biologics for treatment of serious or life-threatening disease or of conditions for which few if any effective therapies exist to reach U.S. markets utilizing surrogate endpoints or following completion of only one clinical trial provided confirmatory studies are completed post-marketing.²¹

Unlike the efficacy determination, which is both specified by statute and generally agreed upon, the criteria used to determine whether a new product is "safe" do not appear in any regulation and are generally not agreed upon.²² For this reason, the decision whether to approve a new prescription drug or biologic is a function of the individual medical officer's assessment of the balance between the efficacy and safety data submitted by the sponsor in the application. This determination is inherently subjective. The primary medical reviewer's decision must go up the regulatory approval chain of command, and may be modified at any point up to the Center Director, or on rare occasions, the FDA Commissioner.²³ Two important points must be made. First, except in rare cases where a sponsor is planning to make a superiority claim for their product against an existing product, most clinical trials test the new drug or biologic against a placebo. Second, because of the limited numbers of patients in large clinical trials (almost always fewer than 5000 subjects) and the relatively short length of most clinical trials, it is virtually impossible for uncommon adverse safety events²⁴ to be detected, or for long-term safety issues to be addressed in any drug or biologic approval.

These efficacy and safety shortcomings are more problematic,

²⁰ *Id.*

²¹ 21 C.F.R. § 314.500 (allowing for accelerated approval of products to treat serious or life threatening illnesses with meaningful therapeutic benefit over existing treatments); 21 C.F.R. § 314.510 (requiring the surrogate endpoint to be reasonably likely to predict clinical benefit and completion of post-marketing studies to verify the surrogate marker effect).

²² Mathieu, *supra* note 19.

²³ See Richard A. Merrill, *Risk-Benefit Decision-Making by the Food and Drug Administration*, 45 GEO. WASH. L. REV. 995 (1976).

²⁴ Louis Lasagna, *Discovering Adverse Drug Reactions*, 249 JAMA 2224 (1983).

and potentially greater, for many new predictive drug adverse reactions and personal genetic medical tests because these medical products are classified and regulated as medical devices.²⁵ The original definition of a medical device was provided in the 1938 Federal Food, Drug, and Cosmetic Act (FDCA).²⁶ Though modified slightly in the past seventy years, the key distinction between a drug and a device has always been preserved. Classification of a predictive medical genetics test as a medical device is of enormous importance, as it means that the standards for efficacy, safety, marketing, advertising, and promotion will be different, and generally more lenient, than those for new drug or biologic approval.²⁷

A. Devices are Categorized by Class, Based on Safety Risk to Consumers, and FDA Approval May be Easier than for Drugs or Biologics

The basic framework for medical device classification and the routes to marketing approval were incorporated into the FDCA by the innovative Medical Device Amendments of 1976.²⁸ Medical devices are classified into three classes based on their potential safety risks, as well as the potential benefits of the device. Class I devices are those which FDA deems to require the least regulatory oversight and as such are subject only to the FDCA's general controls for devices. These general controls are the basic FDA regulatory mechanisms, such as good manufacturing practices (GMPs), registration, and the general FDCA prohibitions against misbranding (e.g., the labeling cannot be false or misleading in any particular), and adulteration (e.g., the device cannot contain substandard materials). Class I devices may be introduced directly into U.S. commerce

²⁵ 21 U.S.C. § 360k(a). See also U.S. FOOD AND DRUG ADMINISTRATION, FDA Consumer Magazine, *Genomics and Medical Devices: A New Paradigm for Health Care*, November-December 2005, available at http://www.fda.gov/fdac/features/2005/605_devices.html (last accessed November 13, 2007).

²⁶ 1938 Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321(h) (2008) (originally enacted as Act of June 25, 1938, Ch. 675 § 201, 52 Stat 1040).

²⁷ Hutt Casebook, *supra* note 16.

²⁸ Medical Device Amendments of 1976, 21 U.S.C. § 360(k)(a).

without submitting a marketing application to the FDA.²⁹ Class II medical devices require more than the general FDCA controls to ensure safety and effectiveness because of their increased safety risk. Special controls the FDA may establish for these devices, in addition to the required general controls, include post-marketing surveillance and device performance standards.³⁰ Failure to comply with a special control, such as a performance standard, renders a Class II device adulterated. Examples of Class II devices are scanning devices such as CT, MRI, or PET scanners. Most Class II medical devices are introduced into the U.S. market via the 510(k) clearance mechanism—a more abbreviated marketing approval mechanism than the more complicated PMA (pre-marketing approval) application which requires extensive new safety and efficacy data.³¹ A few class II devices may be marketed without submission of a marketing application to FDA.

Class III medical devices are defined as those: (1) for which general controls and special controls would not provide reasonable assurance of safety and effectiveness; and (2) which are either for (a) a use in supporting or sustaining human life, or (b) for a use which is of substantial importance in preventing impairment of human health, or (c) which present a potential unreasonable risk of illness or injury.³² Because of their inherently greater safety risk or use in life-saving situations, new Class III medical devices for which no substantially equivalent medical device (predicate device) existed on the U.S. market prior to May 28, 1976 can only be marketed after approval of a PMA; otherwise a 510(k) clearance may be used.³³ Examples of Class III medical devices include coronary artery stents and other medical devices which are permanently implanted in the human body.

The classification of a medical device can be somewhat arbitrary. For example, metallic biliary stents are approved for treatment of

²⁹ 21 U.S.C. § 360 (l).

³⁰ *Id.*

³¹ 21 U.S.C. § 360c(a)(1)(c).

³² *Id.*

³³ *Id.*

cancer-related bile duct obstruction, and as such have been cleared by FDA as Class II devices through review of pre-market notification (510(k)) submissions containing only in vitro bench testing. By contrast, coronary artery vascular stents which are very similar in design and construction are Class III devices only approved following submission of PMA applications containing extensive pre-clinical and clinical trial data.³⁴

Diagnostic kits for genetic testing are also regulated by FDA as medical devices. On first glance, one would assume that such complicated predictive genetic tests should all be regulated as Class III devices because of their complexity, the possibility of making dramatic health-related decisions based on their use, and the lack of pre-1976 predicate devices. However, by federal rule almost all such predictive genetic tests are not Class III devices but rather are classified as either Class I or Class II devices, and subject to less stringent regulatory requirements.³⁵ This non-uniform classification particularly applies to those genetic tests which employ analyte-specific reagents (ASRs) in-house (so called “home brew” diagnostic tests) which are either Class I or II medical devices and which the FDA exercises less regulatory control over than many other kinds of medical devices. A very small number of predictive medical tests are classified, and regulated, as Class III medical devices (e.g., tests for detection of HIV), but essentially all predictive personal genetic tests are not Class III devices. Some of the implications of the way predictive genetic testing kits are classified will be discussed in Section IV.

B. The Route to Market has Significance for Predictive Genetic Medical Device Data Requirements as well as for Advertising to Consumers

The classification of predictive genetic tests as medical devices is not only important because of the extent of jurisdiction and

³⁴ *Marketing or Medicine: Are Direct-to-Consumer Medical Device Ads Playing Doctor?*: Hearing before the Senate Special Committee on Aging, 110th Cong. 1 (2008) [hereinafter Schultz statement] (Statement of Daniel Schultz, M.D., Director, Center for Devices and Radiological Health), http://www.aging.senate.gov/hearing_detail.cfm?id=303085.

³⁵ 62 Fed. Reg. 62, 243 (1997); *see also* 62 Fed. Reg. 62, 244-46 (1997).

regulatory control the FDA has over them, but also because it determines the routes such devices have for access to U.S. markets and consumers. Medical device class allows for dramatic differences in data required to prove safety and efficacy prior to marketing, and affects the level of pre-marketing oversight over direct-to-consumer advertising and promotion of such genetic tests.

New medical devices may enter the U.S. market for promotion and sale to consumers either directly (essentially bypassing the FDA), via an abbreviated marketing application called a 510(k) clearance, or through the submission of a more complicated approval application called a PMA. To a large degree the route to market for a new medical device depends on how CDRH classifies it. It is the responsibility of the manufacturer to determine and select the appropriate class for a new medical device and to petition FDA for such classification. As noted, new Class I devices do not require submission of a marketing application to FDA. Some new Class II medical devices may also be marketed without submitting a marketing application to FDA, but many will enter the U.S. market through the 510(k) clearance pathway if the manufacturer can demonstrate that the proposed new medical device is substantially equivalent to at least one similar predicate device already on the market. A predicate device can be either a Class I, II, or III device previously cleared via an approved 510(k), or a pre-1976 Medical Device Amendment device; that is, a Class II or III device which was already in the U.S. market before the 1976 MDA was passed and for which FDA has not yet called for submission of a PMA. Importantly, the predicate medical device to which a newer device is being compared for marketing approval purposes need not be the "gold standard" device. Nor is there any guarantee that the similarities between the two devices will be great. Lastly, the penultimate approval decision for a medical device, including predictive genetic tests, may not be made by a physician at all but rather by an engineer.³⁶

Because of a combination of administrative (i.e., CDRH) preference, limited FDA resources, the already substantial number

³⁶ Any physician who has ever worked at FDA as a medical officer at CDER or CBER would likely be aware of this. This fact is not noted on any of the official FDA websites.

and range of medical devices on the U.S. market prior to 1976, and the backlog of calls for submission of PMAs for Class III medical devices which previously reached the market via 510(k) clearance, the overwhelming majority of Class II and Class III medical devices have been marketed via the 510(k) clearance pathway.³⁷ This fact is important in the context of any discussion on the advertising and promotion of such medical products directly to consumers because of the significant differences in the amount of safety and efficacy information which must be submitted to the FDA in order to get the medical device either cleared (510(k)) or approved (PMA) for sale to consumers.

The differences in data requirements have narrowed over time as the 510(k) clearance mechanism has been used for progressively more complicated and dangerous medical devices, which have progressively less resemblance to already marketed predicate devices. In general, the 510(k) clearance pathway involves less time for approval, less FDA investment of medical review resources, less submission of original, new-device-specific clinical trial data (in most cases *no* clinical trial data in humans is ever provided), and on occasion, no new safety data. There is thus less device-specific safety and efficacy data to tell the consumer about in an advertisement. Unless a physician or a consumer was aware of the safety and efficacy data for the predicate medical device or the differing (and differences between) marketing mechanisms for new medical devices, it is highly unlikely that anyone would be aware that an advertised or promoted medical device might have been approved for sale and advertising directly to consumers without any substantive safety or clinical effectiveness data being submitted to the FDA.

This situation is made worse by the FDA's self-imposed limited jurisdiction (under the color of enforcement discretion) over medical devices known as "home brew" genetic testing kits, almost all of which are classified as either Class I or Class II medical devices.³⁸ The

³⁷ Hutt Casebook, *supra* note 16, at 994. From 2000-2004 CDRH/FDA received 20,652 pre-market notifications claiming substantial equivalence. *Id.* In the same period the FDA made 338 approval decisions on original PMAs. *Id.*

³⁸ See FDA, Overview of Device Regulation,

consumers to whom these medical devices are directly advertised are likely unaware that the FDA is not involved in quality manufacturing control or efficacy testing, and that the science behind many of the claimed associations between genetic information and clinical characteristics remains tenuous or unsubstantiated. This paucity of data has serious implications in the context of direct-to-consumer advertising and promotion of medical devices, as well as public safety. It is more difficult for claims made to consumers about a medical device's safety or effectiveness to be truthful, yet misleading, if there is little original data to support the claims, the claims are "derived" from claims for another device, and consumers are unaware of the data for the predicate device. This is particularly important when one considers personal genetic information testing, where individuals may make life-altering medical decisions based on genetic testing with little uniform quality control, independent verification of the veracity of the information, or formal input from the medical profession about the strength of the alleged statistical association between the clinical condition being screened for and the results obtained from a home-brew genetic testing kit.

C. The Restricted Medical Device and Predictive Genetic Tests

Adding to the potential confusion are the additional categories of a "restricted" medical device and a prescription medical device. A prescription medical device is one which has been approved for marketing via the PMA process or 510(k) clearance mechanism and which is deemed safe for use by the FDA only when administered under the supervision of a licensed practitioner (physician).³⁹ Some Class II and virtually all Class III medical devices are prescription medical devices.

In the past, the FDA declared that all prescription medical devices would be deemed restricted medical devices, but this position was rejected by the courts.⁴⁰ One way to view restricted medical devices is as a subset of prescription medical devices because

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/default.htm>.

³⁹ See generally FDA, Overview of Device Regulation, *supra* note 38.

⁴⁰ Becton Dickinson v. FDA, 589 F.2d 1175, 1181 (2nd Cir. 1978).

a prescription device may or may not be a restricted device.⁴¹ It is better to think of restricted devices as analogous to prescription drugs even though the statute is crafted in such a way as to give the FDA, through the Secretary of HHS, more flexibility in restricting its use or distribution.⁴² Medical devices may become restricted in one of three ways.⁴³ A restricted medical device is a medical device which can only be sold, distributed, used or ordered (1) upon the written or oral authorization of a practitioner licensed by law to administer or use such a device (i.e. based on a valid prescription written by a physician); or (2) upon other conditions, which might be set by the Secretary of Health and Human Services in a regulation if, because of its potentiality for harmful effect or the collateral measures necessary for its use, there cannot otherwise be reasonable assurance of its safety and effectiveness.⁴⁴ This can occur in two ways: either a condition of approval of a Class III device that its sale and distribution be restricted, or as part of a performance standard requiring that the sale and distribution of the device be restricted.⁴⁵

Most, but not all, restricted medical devices are Class III devices, because Class III devices are either prescription devices or their distribution is restricted as a condition of PMA approval.⁴⁶ However, there are exceptions. For example, diagnostic kits for genetic testing which employ analyte-specific reagents (ASRs) in house (so called "home brew" diagnostic tests), are regulated by the FDA as restricted medical devices even though they are, perhaps inappropriately, classified by the FDA as Class I or II devices. What this means is that a predictive genetic test should, under federal law, be performed only on order from a physician. Some state law reflects this as well.⁴⁷

⁴¹ FDCA § 502(e)-(f); 21 U.S.C. §§ 352(f), 360j(e).

⁴² *Am. Pharm. Ass'n v. Weinberger*, 377 F. Supp. 824, 830 (D.C. Cir. 1974).

⁴³ Schultz statement, *supra* note 34, at 3.

⁴⁴ FDCA § 520(e).

⁴⁵ *Id.*; FDCA § 514(a)(2)(B)(v).

⁴⁶ See FDA, Inspections Compliance Enforcement and Criminal Investigations, <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/default.htm>.

⁴⁷ Genetics & Pub. Pol'y Ctr., *Survey of Direct-to-Consumer Testing Statutes and Regulations* (June 2007) [hereinafter DTCA state law survey], available at

However, the applicability of the “restricted” category on the ordering of a predictive genetic test classified as a medical device depends, at the federal level, on whether the device is one which the FDA has jurisdiction over.⁴⁸ For most predictive genetic tests already being marketed to U.S. consumers, FDA oversight and regulation is limited by the FDA’s decision to regulate the contents of the home-brew tests but not the laboratories themselves. Home-brew laboratories can easily get around state laws, which require the formal involvement of medical professionals for either writing a prescription for the test or counseling patients about test results by claiming that the testing is intended to provide education and information, not a diagnosis.

IV. HOME-BREW TESTING EXCEPTION: THE SIGNIFICANT REGULATORY GAP AND PROBLEM FOR THE FDA AND CONSUMERS

A. CLIA and FDA Jurisdiction over Predictive Genetic Testing Kits

Home brews and commercial genetic testing kits are regulated by the Center for Medicare and Medicaid Services (CMS) under the 1988 Clinical Laboratory Improvement Amendments (CLIA).⁴⁹ CLIA regulations set out the criteria under which the Department of Health and Human Services assigns an in-vitro diagnostic test (such as a personal genetics testing kit) to a “complexity category,” which determines the level of regulatory oversight over the laboratory and its testing service. Predictive genetic tests and other laboratory tests are assigned to complexity categories of simple, moderate, or high complexity. Tests in the “simple” category are subject to the least regulation, whereas tests in the moderate or high complexity

<http://www.dnapolicy.org/resources/DTCStateLawChart.pdf>.

⁴⁸ At the state level this is not a concern, so the issue for getting around the prescription requirement for ordering a genetic test does not center on FDA jurisdiction but rather on what the test is being offered for, i.e. is it educational and informative or diagnostic. This will be explored in the final section of this paper.

⁴⁹ Clinical Laboratory Improvement Amendments (CLIA), Pub. L. No. 100-578 (1988).

categories “must meet regulatory standards dealing with personnel, proficiency testing, quality assurance, and inspections.”⁵⁰ Despite CLIA’s role as the tip of the federal regulatory spear, the FDA also has several assigned roles in the regulation of predictive genetic testing. First, the FDA has the responsibility for determining the complexity category of a medical device testing kit.⁵¹ If the FDA decides that a particular test is “simple” by virtue of having “an insignificant risk of an erroneous result” under CLIA, the laboratories performing these tests may obtain a Certificate of Waiver and be subject to less regulatory oversight.⁵² The jurisdiction over the complexity category determination of a genetic test was also transferred to the FDA from the CDC so that manufacturers who do not market home-brew diagnostic kits, and thus will have to go through the entire gamut of pre-marketing evaluation by the FDA, can do so under the same agency.⁵³

Although the FDA regulates all diagnostic kits as medical devices, regardless of the medical device class category (I, II, or III) assigned to a diagnostic kit by the FDA, the critical distinction from a regulatory point of view is whether the diagnostic genetic kit is

⁵⁰ Lars Noah, *LAW, MEDICINE, AND MEDICAL TECHNOLOGY: CASES AND MATERIALS* (2002) (Chapter 11 on Evolving Medical Technologies contains an excellent discussion of the overlapping jurisdiction CLIA and FDA have over genetic testing) [hereinafter *NOAH CASEBOOK*].

⁵¹ FDA, CTR. FOR DEVICES & RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY & FDA STAFF, ADMINISTRATIVE PROCEDURES FOR CLIA CATEGORIZATION (May 7, 2008), <http://www.fda.gov/cdrh/oivd/guidance/1143.html> (last visited Jan. 23, 2009).

⁵² FDA, CTR. FOR DEVICES & RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY & FDA STAFF, RECOMMENDATIONS FOR CLINICAL LABORATORY IMPROVEMENT AMENDMENTS OF 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices (Jan. 30, 2008), available at <http://www.fda.gov/cdrh/oivd/guidance/1171.html> (“The Secretary of Health and Human Services has delegated to FDA the authority to determine whether particular tests are ‘simple’ and have ‘an insignificant risk of an erroneous result’ under CLIA and thus eligible for waiver categorization (69 FR 22849, April 29, 2004). The Centers for Medicare and Medicaid Services (CMS) is responsible for oversight of clinical laboratories, which includes waiver certificates. CLIA requires that clinical laboratories obtain a certificate before accepting materials derived from the human body for laboratory tests. 42 U.S.C. § 263a(b).”).

⁵³ FDA, CTR. FOR DEVICES & RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY & FDA STAFF, ASSESSING THE SAFETY AND EFFECTIVENESS OF HOME-USE IN VITRO DIAGNOSTIC DEVICES (IVDS): DRAFT POINTS TO CONSIDER REGARDING LABELING AND PREMARKET SUBMISSIONS (Oct. 1988), available at <http://www.fda.gov/cdrh/ode/odecl1272.html>.

considered a “home brew” test⁵⁴ or not. More to the point, the issue is whether the manufacturer of a medical diagnostic kit elects to pursue the “home brew” route for marketing. The FDA requires pre-marketing approval (production quality, test accuracy, and efficacy and safety determinations) for diagnostic test kits sold to clinical laboratories, hospitals, and doctors; the FDA regards these testing kits as medical devices subject to full FDA regulatory authority. On the other hand, if a laboratory test (such as a genetic risk screening test) is developed in-house (for example purely the result of researchers working for a medical school using their own analyte-specific reagents (ASRs—the active ingredients of the in-house developed test⁵⁵) and elects to market this screening kit as a “service,” then the entire FDA pre-marketing approval process, with all its attendant safeguards, is circumvented.⁵⁶ By not providing oversight over these home-brew tests, however, the FDA claims it is exercising what it calls its “regulatory discretion.” The practical result is that the FDA is allowing these testing kits on the market without having to undergo *any* pre-marketing FDA evaluation for safety, effectiveness, accuracy of the testing itself for its claimed benefit,⁵⁷ consistent and high-quality manufacturing practices, or pre-marketing evaluation of the content and truth of the advertising and promotion consumers will be exposed to. Because the FDA only regulates the ASRs (reagents used), *not* the laboratories themselves or

⁵⁴ This term has been used at several points in this paper but now needs to be defined. The term “home brew” refers to reagents, which are manufactured and used within the same facility, yet made available to the public. These companies use their own reagents and use them only in-house, and in the past used to sell the testing service to primary care physicians, though this has changed in the past several years.

⁵⁵ FDA, CTR. FOR DEVICES AND RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY AND FDA STAFF, IN VITRO DIAGNOSTIC (IVD) DEVICE STUDIES—FREQUENTLY ASKED QUESTIONS, DRAFT GUIDANCE (Oct. 25, 2007), *available at* <http://www.fda.gov/cdrh/oivd/guidance/1587.html>.

⁵⁶ FDA, CTR. FOR DEVICES AND RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY AND FDA STAFF, COMMERCIALY DISTRIBUTED ANALYTE SPECIFIC REAGENTS (ASRS: FREQUENTLY ASKED QUESTIONS) (Sept. 14, 2007), *available at* <http://www.fda.gov/cdrh/oivd/guidance/1590.html> (last visited Jan. 23, 2009).

⁵⁷ *FDA to Regulate New Types of “Home Brew” DNA Tests*, WASH. G-2 REP., Sept. 25, 2006, *available at* http://www.g2reports.com/issues/NIR/2006_19/1609937-1.html (last visited Jan. 23, 2009).

the genetic screening test services they provide, there is an enormous regulatory black hole into which many genetic tests now fall.⁵⁸ In effect, the entire regulatory weight of the FDA is designed to protect the public from false claims and ineffective or inaccurate medical testing kits by ensuring that all of the critical aspects of the product meet certain standards. These standards are lifted if a medical device, in particular a genetic testing kit, is considered to be a “home brew” kit. Home brew tests are not marketed commercially (as opposed to being sold directly to individual consumers) and never leave the laboratory where they are manufactured.

The market for “home brew” testing has exploded over the past decade.⁵⁹ The array of conditions and diagnostic information that may be provided to consumers, the complexity of the tests themselves, the level of precision and prognostic/predictive personal information which may be provided to individual consumers as a much more individualized, “personalized” medical product (or service), and the manner in which they are now advertised and promoted directly to consumers have all expanded greatly.⁶⁰ For those predictive testing kits that are not home brew, and thus must go through the FDA’s pre-marketing approval process, the FDA has taken steps to expedite the approval process, particularly for personal genetic testing.⁶¹ The FDA has also made efforts to assert more guidance and regulatory control over testing kits designed to evaluate the ability of an individual patient to metabolize certain drugs and develop certain adverse reactions.⁶² The problem is not the

⁵⁸ NOAH CASEBOOK, *supra* note 50 (“In 1996, labs performed more than 175,000 genetic tests, and the statistics suggest that testing is growing at the rate of 30 percent each year. Tests for more than 400 genetic tests are already available, and an additional 330 tests are in the pipeline.”); see also Rick Weiss, *Ignorance Undercuts Gene Tests’ Potential*, WASH. POST, Dec. 2, 2000, at A1.

⁵⁹ *Id.*

⁶⁰ 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, 1220-29 (1997).

⁶¹ FDA, CTR. FOR DEVICES & RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY & FDA STAFF, PHARMACOGENETIC TESTS AND GENETIC TESTS FOR HERITABLE MARKERS (2007), available at <http://www.fda.gov/cdrh/oivd/guidance/1549.html>.

⁶² FDA, CTR. FOR DEVICES & RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY & FDA STAFF, CLASS II SPECIAL CONTROLS GUIDANCE DOCUMENT: DRUG METABOLIZING ENZYME

FDA-approved testing kits because they comprise such a small percentage of the medical devices now commercially available.

All parties concerned—the FDA, CMS, Congress, and the “home brew laboratories” (which now number in the hundreds or more)—have all become aware that the FDA’s policy of “enforcement discretion” may no longer be working, due in part to the increased public awareness that the majority of the testing kits are home-brews. A second reason is that “personalized” genetic testing kits manufactured and used exclusively “in house” are now being promoted directly to consumers by non-medical personnel and internet-based non-health care organizations without any real involvement by the medical profession and minimal oversight over the medical benefits claimed for these predictive tests. A third reason is that the complexity of the tests has changed. Some of the personal genetic screening kits are no longer just simple tests using ASRs. The tests also involve complicated algorithms (now called In Vitro Diagnostic Multivariate Index Assays) that make statistical calculations, which could potentially create a situation where individual consumers are making life-altering health decisions based on diagnostics that have not had sufficient independent expert verification.

The FDA has recognized, as have attendees at a public meeting on these newer genetic predictive tests,⁶³ that these newer personalized genetic screening kits are a quantum leap in medical informatics and may require a more active, non-discretionary role by FDA.⁶⁴ The concerns are that there are no longer sufficient regulatory provisions guaranteeing safe and effective genetic testing in the U.S.⁶⁵

GENOTYPING SYSTEM (Mar. 10, 2005), *available at* <http://www.fda.gov/cdrh/oivd/guidance>.

⁶³ FDA, CTR. FOR DEVICES & RADIOLOGICAL HEALTH, OFFICE OF IN VITRO DIAGNOSTIC DEVICE EVALUATION AND SAFETY, PRESENTATION: COMMENTS ON FDA’S DRAFT IVMDIA GUIDANCE DOCKET No. 2006D-0347, *available at* <http://www.fda.gov/cdrh/oivd/meetings/020807/Hogarth.html> (last visited Jan. 23, 2009).

⁶⁴ FDA, CTR. FOR DEVICES & RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY, CLINICAL LABORATORIES, & FDA STAFF, IN VITRO DIAGNOSTIC MULTIVARIATE INDEX ASSAYS (July 26, 2007), *available at* <http://www.fda.gov/cdrh/oivd/guidance/1610.html>.

⁶⁵ NATIONAL HUMAN GENOME RESEARCH INSTITUTE, PROMOTING SAFE AND EFFECTIVE GENETIC TESTING IN THE UNITED STATES, APPENDIX 2: RESPONSE OF THE TASK FORCE TO THE FOOD AND

and that the information contained in direct-to-consumer advertising and promotion of such personalized genetic testing services is inadequate. Two of the most recent phenomena in such testing illustrate these legitimate concerns.

V. REGULATORY PROBLEMS WITH TWO NEW HOME BREW PREDICTIVE GENETIC TESTS

A. Predictive Prenatal Genetic Testing by Academic Medical Centers

Baylor College of Medicine in Houston, Texas has an ongoing prenatal genomic testing program, which offers an extensive screening array of fetal DNA fragments using microarray comparative genomic hybridization. This is a cutting-edge technique that allows scientists to scan parent and fetus genomes to rapidly identify copy number variations. The results are read automatically by a laser scanner and analyzed by a computer with special software.⁶⁶ Baylor is one of two medical schools using this new predictive genetic screening technology to scan the DNA of fetuses to “determine if they have any copy number variations that have been associated with disease, or whether they possess novel copy number variations that might cause disease.”⁶⁷

This type of fetal predictive genetic screening is not cheap—Baylor charges roughly \$1600 for the test.⁶⁸ This cost may not be entirely covered by a pregnant patient’s insurance. The medical school derives revenue from this genetic testing and also owns Spectral Genomics, a company that markets arrays to the public similar to those Baylor uses in its research, but charges more than Baylor for the genetic screening.⁶⁹ This new technology is a revenue

DRUG ADMINISTRATION 195 PROPOSED RULE ON ANALYTE SPECIFIC REAGENTS, *available at* <http://www.genome.gov/10002395> (last visited Jan. 23, 2009).

⁶⁶ Bridget M. Kuehn, *Prenatal Genome Testing Sparks Debate*, 300 JAMA 1637 (2008).

⁶⁷ *Id.*

⁶⁸ *Id.*

⁶⁹ *Id.*

engine for a medical school that has recently had a series of widely-publicized financial setbacks.⁷⁰

“Home brew” predictive genetic tests raise certain concerns. First, there is the obvious potential financial conflicts of interest, and possible breach of fiduciary duty to both the mother and fetus. When the physicians who have a significant financial investment in the home-brew genetic testing kits are the same physicians who not only order the testing but are also referred patients from other physicians for counseling about whether they should have prenatal genetic testing at all, there is a financial conflict. Second, even though an academic institution such as Baylor has the enormous advantage of being able to provide expert genetic counseling to patients, on a more clinical level it is not clear whether consumers truly understand that testing often identifies variants of unknown clinical significance, and that many of the potentially harmful variants are rare and have not been well-studied.⁷¹ Prenatal testing of an unborn child’s genome from fetal blood obtained either by amniocentesis or chorionic villus sampling may result in unnecessary termination of pregnancies by anxious parents lacking skilled genetic counseling to interpret ambiguous genetic information.⁷² In the circumstances of genetic data uncertainty, the fiduciary duty to protect the welfare of the fetus may be compromised if care is not taken to prevent parents from terminating pregnancies because of concerns over information that is neither useful nor readily interpretable.⁷³ Statements that “95% of the time you are dealing with pretty black-and-white information” will not be reassuring to anxious parents vulnerable to fears that the genetic information “might” indicate a serious condition even if it is explained to them that the information is of questionable clinical significance.⁷⁴ One could seriously question the ethics of testing for

⁷⁰ *Id.*

⁷¹ *Id.*

⁷² *Id.*

⁷³ The Associated Press, *Some doctors still cautious of gene tests. Experts warn some results may not be useful - and other are 'rubbish', available at <http://www.msnbc.msn.com/id/24473071/print/1/displaymode/1098> (last visited May 6, 2008).*

⁷⁴ Todd Ackerman, *Fetal DNA test sheds light, but stirs an ethical battle*, HOUSTON CHRON.,

harmful or potentially harmful genetic variants in a clinical setting, as opposed to purely research setting, when physicians have no substantive or definitive information about the clinical prognosis of unborn children with such variants as part of a larger array.⁷⁵

It is most bothersome that some of the predictive screening claims which have already been made for Baylor's fetal genetic screening tests are not entirely true.⁷⁶ Public claims that fetal genetic screening may allow parents to know prior to birth whether their child is more likely to have autism or develop schizophrenia later in life, are at best merely hinted at by recent reports,⁷⁷ but are neither substantiated by definitive medical literature,⁷⁸ nor sufficient to allow pregnant couples to make truly informed decisions about the fate of their child. There has been a conspicuous lack of formal criticism of these academic, medical, fetal, predictive genetic screening programs in the medical literature and a clear lack of negative commentary by medical experts on some of the unsubstantiated claims made for the microarray fetal genetic testing program regarding autism and schizophrenia.⁷⁹

December 21, 2008 at A1, available at <http://www.chron.com/disp/story.mpl/moms/6175797.html>.

⁷⁵ See Henry T. Greely, *Genotype Discrimination: The Complex Case for Some Legislative Protection*, 149 U. PA. L. REV. 1483, 1493-97, 1500 (2001).

⁷⁶ Ackerman, *supra* note 74.

⁷⁷ The Associated Press, *Gene sweep yields autism clues. Variety of mutations keep brain from forming proper connections*, July 10, 2008, available at <http://www.msnbc.msn.com/id/25625510/print/1/displaymode/1098> (last visited July 10, 2008).

⁷⁸ William D. Graf et. al., *Autism Associated With the Mitochondrial DNA G8363A RNAllys Mutation*, 15(6) J. CHILD. NEUROL. 357 (2000). See also Paul A. Offit, *Vaccines and Autism Revisited - The Hannah Poling Case*, 358 N. ENGL. J. MED. 2089 (2008); and Gardiner Harris, *Court Hears More Claims of Vaccine-Autism Link*, THE N.Y. TIMES, May 13, 2008, at A1.

⁷⁹ Ackerman, *supra* note 74.

B. Purely Commercial, Non-Medical Genetic Testing⁸⁰

The combination of completion of the human genome project,⁸¹ rapid advances in genetic testing, gene sequencing technology, and the Internet have allowed genetic screening to move entirely out of the physician's office and into the commercial marketplace.⁸² We now have direct-to-consumer promotion and sale of personal genome information and testing⁸³ that is no longer "medical" in several ways: it is not administered under the guidance of physicians, it is invariably unaccompanied by any professional counseling as to what the sequencing data means, and it is no longer promoted only by trained health care personnel or medical institutions.⁸⁴ This is markedly different from the commercial, but clearly medical-based, predictive genetic testing and accompanying counseling services offered by non-medical school affiliated commercial organizations. For example, Myriad Labs in Salt Lake City, Utah, markets an extremely successful menu of home-brew genetic screening testing designed to allow women with a family history of breast or ovarian cancer to determine their relative risk of developing these diseases based on the degree of expression of the BRCA family of genes.⁸⁵

As a result of public marketing, genetic testing is no longer confined to the simple evaluation of serum or amniotic fluid for specific chromosomal abnormalities in order to detect the presence of

⁸⁰ Some of this material was previously published by the author in *Health Law Perspectives*, a biweekly electronic health law newsletter of the Health Law and Policy Institute at the University of Houston Law Center. Bruce Patsner, *Direct to Consumer Genetic Testing: Think Before You Spit*, *Health Law Perspectives* (Nov. 2008), available at <http://www.law.uh.edu/healthlaw/perspectives/homepage.asp>.

⁸¹ Elizabeth Pennisi, *Human Genome: Reaching Their Goal Early, Sequencing Labs Celebrate*, 300 *SCIENCE* 409 (2003).

⁸² Jennifer A. Gniady, *Regulation of Genetic Testing*, 76 *FORDHAM L. REV.* 2429 (2008).

⁸³ Ron Winslow, *Is There a Heart Attack in Your Future? Genetic Tests Promise to Map Your Personal Health Risks, But Some Question Usefulness*, *WALL ST. J.*, Nov. 6, 2007.

⁸⁴ Phyllis Griffin Epps, *Thoughts on the Prospect of Elective Comprehensive Genome Screening*, *Health Law Perspectives* (December 23, 2002), available at <http://www.law.uh.edu/healthlaw/perspectives/Genetics/021223Thoughts.html>.

⁸⁵ MA Blackwood & BL Weber, *BRCA1 and BRCA2: from molecular genetics to clinical medicine*, 16 *J. CLIN. ONCOL.* 1969 (1998).

a specific disease, such as Tay-Sachs disease,⁸⁶ nor is it limited by even the most advanced prenatal genomic testing such as that now being marketed by some medical centers for earliest possible detection of the widest array of genetically-based diseases or genetically-linked medical conditions.⁸⁷ Nor is the goal confined to the screening of higher-risk patient populations to determine whether there is a greater chance of developing a malignancy which might be prevented with early intervention.⁸⁸ The latest commercial trend is the genetic “spit party.”⁸⁹ For a fee ranging from \$400 to \$2500 or more, apparently healthy individuals can provide a sample of their saliva to a sponsor⁹⁰ who then sends the fluid to a commercial laboratory to test the entire genome for thousands of variants of select portions of genetic material (known as “snips”) using an in-house, home-brew genetic testing kit, which, as noted, falls outside current FDA regulation. The goal is as much social information as medical. Many participants are not simply interested in whether they have a “predisposition” to, or elevated risk for, developing any of a number of major diseases such as Parkinson’s disease, Huntington’s chorea, or coronary artery disease.⁹¹ Just as important is a “determination” of one’s genetic risk for more benign social traits such as baldness, good looks, intelligence, or a predisposition to depression.⁹² Getting this genetic information is as simple as logging on to one’s account at the start-up company acting as your genetic

⁸⁶ The American College of Obstetricians and Gynecologists, *Prenatal and Preconceptional Carrier Screening for Genetic Diseases in Individuals of Eastern European Jewish Descent*, 298 ACOG COMM. OPINION, (Aug. 2004).

⁸⁷ See Epps, *supra* note 84.

⁸⁸ Alan E. Guttmacher and Francis S. Collins, *Genomic Medicine: A Primer*, 347 N. ENGL. J. MED. 1512 (2002).

⁸⁹ Michael Schulman, *Double Helix Dept. Ptooy!*, THE NEW YORKER, Sept. 22, 2008, at 35.

⁹⁰ There are three for-profit non-medical companies offering this service at the moment in the U.S. They are 23andMe, Decode Genetics, and Navigenetics. See Amy Harmon, *My Genome, Myself: Seeking Clues in DNA*, THE N.Y. TIMES, Nov. 17, 2007, at A1, available at <http://www.nytimes.com/2007/11/17/us/17dna.htm?pagewanted=print>. None of the activities of these companies is regulated by the FDA.

⁹¹ Schulman, *supra* note 89.

⁹² Harmon, *supra* note 90, at A1.

custodian.⁹³ Involvement of the medical profession, even in a counseling capacity, and the need for a prescription to obtain access to personalized, predictive genetic testing kits are no longer required.⁹⁴

It is all a new business, well on its way to becoming a big marketing business which unfortunately is more targeted than the actual genetic testing being done.⁹⁵ The lack of genetic counseling accompanying these commercial, non-medical activities is particularly worrisome, but may be less of an issue because consumers of these services are interested in both social and medical information. Nevertheless, not enough people are thinking about whether the genetic information they are receiving is accurate enough in any meaningful sense to be truly predictive of the "trait" they are looking for.⁹⁶ Worse still, there are serious questions remaining about where their genetic information could end up and who actually owns their genetic data. The long-term consequences of such testing, whether additional, unanticipated and unwanted testing will pop up, or whether this information should be treated differently than other medical information⁹⁷ are also glossed over or remain unanswered by the individuals or organizations sponsoring these "spit parties."

These purely profit-driven, non-medical businesses do avoid the financial conflicts of interest that academic medical centers may have and that patients may not be aware of. However, for non-scientific genetic testing companies, such as 23andMe, who simply have customers interested in the chance to decode their genes,⁹⁸ there is

⁹³ *Id.* "Logging onto my account at 23andMe, the start-up company that is now my genetic custodian, I typed my search into the 'Genome Explorer' and hit return. I was, in essence, Googling my own DNA." *Id.*

⁹⁴ Rick Weiss, *Genetic testing gets personal*, WASH. POST, Mar. 24, 2008, at A1.

⁹⁵ Bridget M. Kuehn, *Risks and Benefits of Direct-to-Consumer Genetic Testing Remain Unclear*, 300 JAMA 1503 (2008).

⁹⁶ Sarah E. Gollust, Sara Chandros Hull, and Benjamin S. Wilfond, *Limitations of Direct-to-consumer Advertising for Clinical Genetic Testing*, 288 JAMA 1762 (2002).

⁹⁷ Mark A. Rothstein, *Genetic Exceptionalism and Legislative Pragmatism*, 35(2) J. L. MED. ETHICS 59, 61 (2007).

⁹⁸ Schulman, *supra* note 89.

the greater problem of independent validation of the quality of the genetic testing equipment, the qualifications of the scientists they employ, the quality of the genetic information given to consumers, and the accuracy of the test results themselves. This is less of a concern when one is dealing with academic medical centers, such as Baylor College of Medicine, or pioneering genetics companies, such as Myriad, who were founded by some of the best genetic sequencing scientists in the United States. For the purely commercial, non-medical genetic screening enterprises, there is currently no way for consumers to know the accuracy of any of the genetic information they are paying significant sums of money to obtain.

C. The Fate of Your Genetic Information

The lack of any meaningful quality control over home-brew genetic testing remains a fairly large hole in the federal regulatory matrix governing medical products and protecting consumers even if some of the consumer concerns about the privacy of their genetic information are met by the Genetic Information Nondiscrimination Act of 2008 (GINA).⁹⁹ The passage of GINA will hopefully ensure that individual genetic information, however obtained, will not be used by insurers and employers in health insurance and employment decisions.

GINA goes a long way towards protecting against corporate abuse of otherwise private personal genetic information, but there are significant limitations on the protections GINA offers. GINA does not apply to life insurance, disability insurance, long-term care insurance, or other uses of genetic information.¹⁰⁰ Nor do GINA's health insurance provisions apply to people who are symptomatic or to "non-genetic" predictive testing and information (also known as epigenetics).¹⁰¹ None of the quality assurance and scientific legitimacy issues posed by the commercialization of genetic screening are addressed by this piece of legislation. There is also nothing in GINA that addresses how purely commercial, non-

⁹⁹ The Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, Stat. 881.

¹⁰⁰ *Id.*

¹⁰¹ *Id.*

medical business enterprises that sponsor genetic testing “spit parties” must deal with their customers’ genetic data. This fact, coupled with the legitimate fear many individuals already have over use of their genetic information,¹⁰² provides further evidence that more regulatory control is needed over the new predictive genetic testing technologies just described.

VI. A GREATER ROLE FOR FDA IS THE SOLUTION

The regulatory concerns about efficacy, safety, manufacturing, quality control, accuracy of results, and promotional claims for the newest generation of home-brew, personalized, predictive genetic testing kits, whether originating in academic medical centers or Internet-based businesses, are legitimate ones.

Recent national conferences on personalized medicine and risk assessment¹⁰³ have recognized some limitations on the FDA’s ability to keep pace with rapid advances in predictive medical technology and highlighted several unpleasant truths about current FDA approval of new medical products and the new diagnostic pharmaceutical predictive technology: (1) the majority of drugs which reach Phase III clinical trials are never approved and an enormous amount of money is wasted in new drug development and inefficient clinical trials;¹⁰⁴ (2) smarter clinical trial design is necessary in order to identify patients more likely to have adverse events;¹⁰⁵ (3) the overall clinical benefit from much pharmacotherapy is unrealized for many patients who take prescription drugs, with a significant number of patients having little effective response to drug therapy;¹⁰⁶ and (4) many of the assumptions underlying traditional FDA regulation of new medical products do not apply since there is so

¹⁰² Amy Harmon, *Fear of Insurance Trouble Lead Many to Shun or Hide DNA Tests*, N.Y. TIMES, Feb. 24, 2008, at A1.

¹⁰³ N. Y. ACAD. OF SCI. PROGRESS IN TOXICOGENOMICS: PERSONALIZING DIAGNOSTICS AND RISK ASSESSMENT, Mar. 27, 2008, <http://www.nyas.org/toxicogenomics>.

¹⁰⁴ *Id.*

¹⁰⁵ *Id.*

¹⁰⁶ *Id.*

much “off-label” use of predictive diagnostic testing which the FDA has little oversight over.¹⁰⁷ All of these concerns are amplified for new predictive genetic testing.

The real cause of these concerns, however, is neither “off-label” uses of FDA-approved predictive personalized medical products for drug adverse reactions or genetic risk, nor unsubstantiated claims by physicians regarding the purported diagnostic benefits of such drug or genetic testing. While these *are* significant problems, the real problem is that the FDA has been cut out of the product development, safety and efficacy evaluation, as well as the regulation of marketing, largely because of the enormous loophole the “home-brew” exception provides to the makers of predictive drug and genetic tests and medical devices.

The numbers, and the market, both reveal that the ubiquity of the “home-brew” exception to FDA jurisdiction is the real problem. The number of marketed predictive medical tests is so much greater than the number of tests that the FDA has actually approved that, in effect, an entire industry of diagnostic drug assays and genetic tests has developed outside the penumbra of FDA regulatory oversight,¹⁰⁸ except on the rare occasion, as noted, when a new predictive diagnostic test does not meet the criteria for a “home-brew” or when a purely commercial manufacturer is seeking formal FDA approval for marketing.¹⁰⁹

¹⁰⁷ Barbara J. Evans, Making Personalized Medicine Work: The Legal and Regulatory Paradigm Shift (presented at N.Y. Acad. of Sci. Feb 4, 2008), in PROGRESS IN TOXICOGENOMICS: PERSONALIZING DIAGNOSTICS AND RISK ASSESSMENT, (Mar. 27, 2008), <http://www.nyas.org/toxicogenomics>.

¹⁰⁸ SEE SECRETARY’S ADVISORY COMM. ON GENETICS, HEALTH, AND SOC’Y, DEP’T OF HEALTH AND HUMAN SERVS., US SYSTEM OF OVERSIGHT OF GENETIC TESTING: A RESPONSE TO THE CHARGE OF THE SECRETARY OF HHS 106 (2008) (citing GeneTests Web site, <http://genetests.org> (last visited Mar. 30 2008)), *available at* http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf. The report pointed out that there were over 1100 genetic tests available but only a few dozen cleared/approved by FDA. *Id.* The number of new predictive genetic tests marketed as “home-brews” and promoted directly to consumers has certainly increased since that time.

¹⁰⁹ Andrew Pollack, *F.D.A. Says Cancer Test Failed to Get Its Approval*, N.Y.TIMES, Oct. 9, 2008, at A1, *available at* http://www.nytimes.com/2008/10/09/business/09cancer.html?_r=1&ei=5070&oref=slogin.

The fact that there are more than 1000 predictive genetic tests available right now to the American public with fewer than several dozen of these medical devices approved or cleared for marketing by the FDA indicates that, for all intents and purposes, the FDA has ceased to be the gatekeeper for public safety in this arena. The numbers would suggest that the FDA's role has been reduced to that of a minor player. Furthermore, there are some conclusions that should be drawn from the existence of such an enormous number of non-FDA approved predictive tests on the market and a conspicuous lack of any litigation against these sponsors for false claims. One conclusion might be that most individual states do not have a grasp on this regulatory problem.¹¹⁰ Several states have tried to limit attempts by personal genome testing companies to advertise their services and claims directly to consumers under the color of state laws that forbid the practice of providing direct medical diagnostic information without the appropriate involvement of a licensed physician.¹¹¹ These laws, however, are easily circumvented by sponsors who can alternatively claim that (1) the predictive genetic information they are providing is intended to be only educational and informative, not "diagnostic" in any traditional medical sense (this is undoubtedly true in many instances since these companies make no effort to provide genetic counseling services to accompany the testing), and (2) the testing is accompanied by a disclaimer that "the information should not be used for diagnosis, treatment, or health ascertainment purposes, and it directs them to their physicians if they have questions or concerns about their health status."¹¹²

¹¹⁰ There are some notable exceptions, though they are notable in part because they are so few and far between. Myriad Genetics Laboratories in Salt Lake City, Utah holds the patents on BRCA-testing for determining the predisposition of an individual woman to develop breast or ovarian cancer. Though the tests were developed to test predilection to develop certain malignancies in women at high-risk because of family history of such diseases, Myriad Labs launched a national direct-to-consumer advertising campaign for these tests which are expensive (a battery of tests can easily run to upwards of \$3000, often not covered by health insurance) and of little value for the overwhelming majority of women exposed to such ads. Though the ads were promoted as educational, the State of Connecticut thought otherwise.

¹¹¹ DTCA state law survey, *supra* note 47.

¹¹² Amy L. McGuire and Wylie Burke, *An Unwelcome Side Effect of Direct-to-Consumer Personal Genome Testing. Raiding the Medical Commons*, 300 JAMA 2669 (2008) [hereinafter McGuire].

The situation is worse than it appears.¹¹³ As noted in the previous section, one should not count on the medical profession to police itself in the area of predictive genetic testing. This is particularly true when such testing promises to serve as a revenue engine for cash-strapped academic institutions, which are now in the position to market cutting-edge predictive genetic technologies to targeted patient populations. The fact that the claims about a predictive genetic test are being made by university medical center professors is no guarantee that the information is totally accurate or even correct.¹¹⁴ One of the few recent FDA successes in attempted regulation of “home-brew” cancer screening tests occurred because the test, and the testing materials, were developed by a medical school rather than the laboratory itself selling the test, and were determined to not be a true home-brew test.¹¹⁵

Whether these new predictive genetic screening tests are sponsored by prestigious medical schools or are purely commercial enterprises,¹¹⁶ the clinical value of some of this personal genome predictive testing information, as well as the core validity of the predictive significance of some of the genetic information claimed for the tests, remains unproven. This is a public health issue that ultimately goes well beyond the confines of whether such advertising is protected commercial speech or whether a disclaimer about the purely informational or educational content of the test results is adequate warning to consumers not to take the findings as absolute until they have had a chance to talk to a knowledgeable health

¹¹³ THE GRATEFUL DEAD, TOUCH OF GREY (Warner Brothers Records 1982).

¹¹⁴ For example, see Chromosomal Microarray Analysis, Baylor College of Medicine, *available at* <http://www.bcm.edu/cma/professional.htm> (last accessed Sept. 22, 2007). Baylor College of Medicine offers microarray analysis as part of its antenatal fetal genetic testing program; the analysis tests the fetus for over 65 disorders or for genomic errors associated with autism or mental retardation even though there is no definitive proof that autism can be accurately screened for by testing of fetal blood prior to birth.

¹¹⁵ See Pollack, *supra* note 109. In this case an ovarian cancer screening test called Ovasure was being marketed by Lab Corp, even though its accuracy had not been tested against the current standard test of serum CA-125 measurement. *Id.* The test was not eligible for a home brew exception, and thus illegally marketed, because the test itself as well as the materials for the test were not developed in house by the laboratory but rather were developed at Yale Medical School by other faculty. *Id.*

¹¹⁶ McGuire, *supra* note 112.

professional.¹¹⁷ At the end of the day, predictive drug and personal genetic predictive tests must be consistent, valid, and proven effective and safe, just as if the products had gone through formal FDA evaluation and approval. The single most important regulatory question which must be answered is who should provide the additional regulatory control over this predictive genetic technology. Although the states and the medical profession have made some efforts in this area, the choice ultimately comes down to either the federal government through expanded FDA action, or the free market. In this author's opinion, most of the arguments and nearly all of the data (at least what exists in the area of direct-to-consumer advertising of medical devices) favor more federal regulation.

A. Federal Government, Not the Market, as the Regulatory Solution

Attempts to increase the FDA control over the home-brew industry have happened before. A Congressional bill to transfer regulatory oversight over such laboratory facilities to the FDA was introduced by Senators Kennedy (D-MA) and Obama (D-Ill.) in 2006, but the bill was not passed.¹¹⁸ Senators Obama and Kennedy's proposed legislation¹¹⁹ recognized the home-brew exception regulatory gap and proposed reform to correct this by shifting responsibility for in house genetic testing to the FDA and expanding its jurisdiction and enforcement powers over this growing industry.¹²⁰ This bill should be introduced again and passed by

¹¹⁷ The data on disclaimers for dietary supplement claims is not encouraging in this regard.

¹¹⁸ Washington G-2 Reports, National Intelligence Report, *Key Laboratory, Pathology Priorities for the New Congress, Expanded Controls on 'Home Brew' Tests*, Jan. 15, 2007, available at http://www.g2reports.com/issues/NIR/2007_1/1611293-1.html (last accessed Oct. 27, 2008).

¹¹⁹ *Id.* The bill introduced by Sen. Kennedy and sponsored jointly by Senators Kennedy and Obama was S. 736, 110th Cong. (2007), "Laboratory Test Improvement Act."

¹²⁰ Blaine Bettinger, *THE GENETIC GENEALOGIST, Government Regulation of Genetic Genealogy Tests*, Mar. 24, 2007, available at <http://posts.blogcarnival.com/page.php?p=50108>. This article posted Sen. Kennedy's news release that clarified his position: "The legislation will mandate that all providers of 'home-brew' laboratory tests provide the FDA with evidence that verifies their analytical and clinical validity. All of the information submitted to the FDA will be compiled into a database, which will subsequently be made available to the

Congress.

The current situation exists because the FDA has been cut out of the regulatory loop. The combination of CMS (through CLIA), the states, and the medical profession have provided a mish-mash of scant regulation, oversight, and enforcement. In the absence of direct FDA involvement and control, it is not clear how proposals for more premarket scrutiny of predictive drug and genetic testing (such as those called for by the Secretary's Advisory Committee on Genetics, Health, and Society) will be accomplished with real regulatory review. More than any other federal or state agency, the FDA alone has the personnel, experience, and expertise to do this, even if the problem of limited FDA resources and personnel is clearly a limiting factor. One advantage of additional FDA involvement is that home-brew genetic testing sponsors could no longer avoid state regulations by claiming that they are providing a "service," and not a diagnosis.

Short of completely eliminating the home-brew exception to FDA rules and regulations, it is unlikely that the average consumer will receive either adequate accurate information or sufficient protection from false or misleading claims without a significant expansion of the FDA's role. An examination of what has happened in the relatively new arena of direct-to-consumer advertising of implantable medical devices provides a lesson about why free markets are likely to fail if they are allowed to continue to regulate home-brew genetic testing sponsors.

B. Market Failure at Regulating Direct-to-Consumer Advertising of Implanted Restricted Medical Devices Demonstrates why More Federal Regulation is Needed¹²¹

The alternative to more federal regulation of home-brew genetic

public on the Internet. Presently, an overwhelming majority of the laboratory tests employed by health care facilities are home-brew tests that have not been approved by FDA. In some instances, home-brew tests are used to diagnose Huntington's disease and susceptibility to breast cancer. As such, the results of homebrew tests affect the lives of thousands of Americans and their families each and every year." *Id.*

¹²¹ Some of the data and text used in this section will also appear in an upcoming publication by the author. See generally Bruce Patsner, *The Problem of Direct-to-Consumer Advertising (DTCA) of Restricted, Implantable Medical Devices: The Current Regulatory Approach Must Be Changed*, 64 FOOD AND DRUG L.J. 2009 (in press).

testing kits through increased FDA action is to allow all of these tests on the market as is. This places the focus on sufficiently educating consumers about new predictive genetic screening technology, allowing them to select reliable predictive commercial genetic tests and companies, creating a preference for superior tests and companies, and effectively discarding those that are inferior (this process functions much like that used when shopping for a used car, assuming people appropriately evaluate used cars). However, the current situation exists in large part because the market has failed as a regulatory force in the arena of personalized genetic testing kits.¹²²

Relying on the free market and a combination of information and disclaimers to control the burgeoning genetic testing industry requires a leap of faith that is inconsistent with the ongoing experience of U.S. consumers in the only other significant area of medical device profitability being directly promoted to them, specifically that of implantable, restricted medical devices. Are consumers educated, and is critical information adequately publicized? The data on direct-to-consumer advertising (DTCA) for restricted implantable medical devices (such as coronary artery stents and orthopedic joint replacements) and consumer comprehension of this information is not encouraging.

The potential consumer educational benefits of medical product advertising aside,¹²³ no one on either side of the DTCA debate disputes that the primary reasons for advertising medical products are to increase consumer demand¹²⁴ and product market share for

¹²² See Andrew Pollack, *A Genetic Test That Very Few Need, Marketed to the Masses*, N.Y. TIMES, September 11, 2007 at C3.

¹²³ S. Gilbody, P. Wilson and I. Watt, *Benefits and Harms of Direct to Consumer Advertising: A Systematic Review*, 14 QUALITY & SAFETY HEALTH CARE 246 (2005). The Pharmaceutical industry claims one of the main benefits of DTCA is patient education. *Id.* At 246, 249. Although there is the potential for DTCA to be educational, the primary benefit is for the manufacturer in the form of increased market share and profits.

¹²⁴ D. John Loden & Caroline Schooler, *How to Make DTC Advertising Work Harder*, MEDICAL MARKETING AND MEDIA, April 1998. A comment by these two DTC advertising executives at FCB Healthworks wrote "The ultimate goal of DTC advertising is to stimulate consumers to ask their doctors about the advertised drug and then, hopefully, get the prescription." *Id.* at 44.

manufacturers, and to distinguish a product from its competitors.¹²⁵ This applies to predictive personalized genetic testing kits as much as it does for coronary artery stents.

Growth of DTCA spending in the U.S. provides some perspective on this statement. After passage of the FDA Modernization Act of 1997 (FDAMA),¹²⁶ growth of DTC spending increased from \$791 million in 1996 to over \$3 billion in 2004.¹²⁷ Research has shown both that consumers are susceptible to directed advertising of drugs,¹²⁸ and that some medical practice is even driven by consumer demand for heavily-promoted pharmaceuticals.¹²⁹ Research has also shown that demand for surgical therapies and devices can be driven, to some degree, by advertising.¹³⁰ Although

¹²⁵ See N.Y. TIMES, July 1, 2008. For example, Myriad Genetics of Salt Lake City initiated a mass direct to consumer advertising campaign for their BRCA genetic testing for predisposition to breast and ovarian cancer which resulted in a doubling of revenue. *Id.* No more than 5-10% of all women in the U.S. could theoretically benefit from such genetic screening, yet the direct-to-consumer advertising campaign did not attempt to discriminate, and was directed at all women. *Id.*

¹²⁶ See generally Food and Drug Administration Modernization Act of 1997 (FDAMA), Pub. L. No. 105-115.

¹²⁷ Judith A. Cahill, Executive Director, Academy of Managed Care Pharmacy, Statement before the Food and Drug Administration Public Hearing on Direct-to-Consumer Advertising, Washington, D.C. (November 2, 2005). It was not stated whether there was a direct cause-effect relationship between the passage of FDAMA and the increase in spending on direct-to-consumer advertising. *See id.*

¹²⁸ See The Henry J. Kaiser Foundation, *Impact of Direct-to-Consumer Advertising on Prescription Drug Spending* 1, 7 (June 2003), <http://www.kff.org/rxdrugs/upload/Impact-of-Direct-to-Consumer-Advertising-on-Prescription-Drug-Spending-Summary-of-Findings.pdf>. The DTC advertising strategy works: "DTC advertising produces a significant return for the pharmaceutical industry: every additional \$1 the industry spent on DTC advertising in 2000 yielded an additional \$4.20 in sales." *Id.* at 7.

¹²⁹ Richard I. Kravitz et al., *Influence of Patients' Requests for Direct-to-Consumer Advertised Antidepressants: A Randomized, Controlled Trial*, 293 JAMA 1995, 1999 (2005).

¹³⁰ M. Jaffe, *HealthpointCapital, Orthopedic and Dental Industry News, Impact of Direct-to-Consumer Advertising*, Apr. 6, 2006, available at http://www.Healthpointcapital.com/research/2006/04/06/impact_of_directtoconsumer_advertising. The article cites research by Orthopedic Surgeon Kevin Bozic of the University of California San Francisco School of Medicine, which was presented at the Health Policy Symposium at the 2006 American Academy of Orthopedic Surgery (AAOS) meeting. *Id.* Dr. Bozic's findings were that 50% of orthopedic surgeons polled said that they "found pressure to use a 'particular surgical technique approach or specific type of implant' by patient request" based on viewing DTCA. Some of the DTCA was internet-based and some television

there is no universally accepted data that demonstrates consumers are directly harmed by DCTA, there is indirect data. There is no reliable evidence suggesting consumers receive any real educational benefit from the direct advertisement of medical devices. In fact, some data suggests that consumers do not really understand the information being conveyed in broadcast promotions for restricted medical devices.¹³¹ If that is the case, and advertising to consumers helps drive demand, little good will come of a situation in which consumers, because they lack expert knowledge, are not in a position to make prudent purchasing decisions.¹³² Virtually all recent peer-reviewed medical literature strongly suggests that consumer-driven health care is not necessarily in patients' best interest.¹³³

In all fairness, some commentators have pointed out that DTCA offers an opportunity for manufacturers to educate consumers about diseases, increase consumer awareness about disease symptoms, inform consumers about treatment options and diagnostic procedures, stimulate patient-physician dialogue on vital health issues, and possibly encourage healthier lifestyles.¹³⁴ Unfortunately, it is difficult to achieve all of these objectives, particularly in the limited time span offered by broadcast media advertisement, because the primary objective of advertising is to promote a specific medical product device or a drug (as opposed to awareness about a particular disease). Where there is promotion and advertising of a specific product, it is possible, and perhaps even more likely, that DTCA will do consumers a disservice.

broadcast. *Id.* Sixty percent of the time patients had an opinion about what should be done surgically before they ever spoke to the surgeon. *Id.*

¹³¹ Direct-to-Consumer Advertising (DTCA) of Angioplasty and Stents for Chronic Angina: Hearing Before the Senate Special Committee on Aging, 110th Cong. 1-18 (Sept. 17, 2008) [hereinafter Boden statement] (statement by William E. Boden, M.D., Professor of Medicine SUNY at Buffalo School of Medicine & Public Health), available at http://www.aging.senate.gov/hearing_detail.cfm?id=303085 (last accessed Sept. 30, 2008).

¹³² Arnold Relman, *McCain, Obama, and the National Health*, THE N.Y. REV. OF BOOKS, Nov. 6, 2008, at 27.

¹³³ See Robert A. Berenson & Christine K. Cassel, *Consumer-Driven Health Care May Not Be What Patients Need – Caveat Emptor*, 301 JAMA 321 (2009).

¹³⁴ Wayne L. Pines, *A History and Perspective on Direct-to-Consumer Promotion*, 54 FOOD & DRUG L.J. 489, 508-09 (1999).

According to a 2002 report by the General Accounting Office (GAO),¹³⁵ the pharmaceutical industry's track record on fair and balanced information in DTCA is not encouraging. Importantly, there is no evidence that the restricted medical device industry's conduct is any better. The conclusions of the GAO report were that (1) DTC advertising appeared to increase drug spending and utilization; (2) DTCA was concentrated among a small number of drugs and conditions rather than directed at sweeping public health issues;¹³⁴ and (3) some manufacturers repeatedly disseminated misleading ads for the same drugs, disregarded repetitive warnings from the FDA, and failed to submit in a timely manner (or at all) newly disseminated ads to the FDA for review. The limitations of FDA oversight of DTCA were apparent to the GAO as well.¹³⁶ Even FDA surveys¹³⁷ on consumer behavior associated with DTCA campaigns for prescription drugs provide further evidence that these concerns are legitimate. Again, this would apply to predictive genetic testing too.

The minimal formal investigation into consumer comprehension of DTCA of restricted medical devices would seem to confirm all of these concerns.¹³⁸ Evaluation of ads for a group of implantable

¹³⁵ UNITED STATES GENERAL ACCOUNTING OFFICE, REPORT TO CONGRESSIONAL REQUESTERS, PRESCRIPTION DRUGS. FDA OVERSIGHT OF DIRECT-TO-CONSUMER ADVERTISING HAS LIMITATIONS, (Oct.,2002), <http://www.gao.gov/new.items/03177.pdf>.

¹³⁴ *Id.* at 4.

¹³⁶ *Id.* at 17-25.

¹³⁷ *Id.* at 28-29 (citing Kathryn J. Aikin, Division of Drug Marketing, Advertising, and Communications, FDA, *Attitudinal and Behaviors Associated with Direct-to-Consumer Advertising of Prescription Drugs: Summary of Survey Results*, FDA Scientific Rounds, Mar. 30, 2005, available at <http://www.cdernet.cder.fda.gov/dtd/Rounds/Fall04/bg3-30.htm> (last accessed Mar. 30, 2005)). DDMAC's survey noted that although DTC ads increase awareness of possible treatments, DTC ads did not convey information about risks and benefits equally well. In particular, it was clear that physicians believe patients understand benefits much better than risks (which is not surprising if more benefit than risk information is presented). The physicians also believed that DTC ads confuse patients about relative risks and benefits of drugs.

¹³⁸ See generally *Direct-to-Consumer Ads for Medical Devices: What Do People Understand and Remember?* Hearing before the Senate Special Committee on Aging, 110th CONGRESS, (Sept. 17, 2008). (Statement of Ruth S. Day, faculty member of Duke University & Director of the Medical Cognition Laboratory), available at http://www.aging.senate.gov/hearing_detail.cfm?id=303085.

medical devices, such as coronary artery stents, knee and hip joint replacements, implantable defibrillators, and breast implants revealed an absence of risk information in many ads, heavy reliance on patient "testimony" as to the merits of the device, and consistent reporting of twice as many benefits as risks, consistent with the same pattern seen in DTCA of prescription drug ads.¹³⁹ Furthermore, because consumers are not used to seeing advertisements for restricted medical devices, particularly implantable ones, and have no information framework for such ads, they lack the reference point for comparison to other ads.

The same general remarks and caveats apply to personalized genetic testing kits as well. Direct to consumer advertising of genetic testing for breast and ovarian cancer risk (BRCA analysis) by established medical genetics companies, such as Myriad Laboratories in Salt Lake City, has already resulted in subpoenas for information from the company¹⁴⁰ and concerns that a test useful for less than 5 percent of the U.S. female population is being fraudulently promoted to millions of women for whom the test has little or possibly no value.¹⁴¹ Noted medical ethicists have pointed out as much.¹⁴² These issues surfaced despite the fact that: (1) much of the advertising and promotional material by this company for BRCA gene cancer risk testing is clearly educational in nature; (2) Myriad is a scientific company which has some of the most renowned genetic testing scientists in the United States on its staff; and (3) their sequencing equipment is state of the art, and their staff, facilities, and equipment testing information are all readily accessible in the public domain.

¹³⁹ *Id.* "Overall, risk information is seriously disadvantaged relative to benefits in medical device ads-the techniques used to present them often render them lower in cognitive accessibility." *Id.*

¹⁴⁰ Andrew Pollack, *A Genetic Test That Very Few Need, Marketed to the Masses*, N.Y. Times, Sept. 11, 2007, available at <http://www.nytimes.com/2007/09/11/business/media/11genetics.html?sep=1&sq=Andrew%20Pollack,%20Genetic%20Test%20That%20Very%20Few%20Need&st=cse>.

¹⁴¹ *Id.*

¹⁴² See Arthur Caplan, *Women Should Be Wary of Cancer Test Campaign: TV Commercials Exploit Fear of Breast Cancer in the Guise of Education*, MSNBC.COM, Sept. 14 2007, <http://www.msnbc.msn.com/id/20761643/print/1/displaymode/1098>.

C. Current Congressional Hearings on DTCA of Medical Devices

Direct-to-consumer advertising of medical devices appeared on the official Congressional radar in September 2008 in a hearing before the Senate Special Committee on Aging,¹⁴³ convened by Senators Herb Kohl (D-WI) and Gordon H. Smith (R-OR) as part of an ongoing fifteen-month series of oversight hearings on medical device and pharmaceutical marketing. The purpose of the committee meeting was to hear testimony of representatives from the medical device industry, physician-surgeons with expertise in medical device advertising, consumer and advertising groups, CDRH/FDA representatives, and academics with extensive clinical research experience in consumer comprehension of medical product advertisements in order to determine whether appropriate risk and safety information about restricted medical devices is being provided to consumers.

The Special Committee appeared acutely aware of the fact that DTCA of restricted medical devices, particularly restricted implanted devices such as coronary artery stents and artificial knees, was a growing but recent phenomenon and one which had yet to be highly scrutinized.¹⁴⁴ With the exception of testimony from the representative of the medical device advertising industry,¹⁴⁵ virtually all of the speakers emphasized the glaring deficiencies in safety risk information and comprehension of such information for consumers viewing DTCA of restricted, particularly implanted, medical devices. The hearing testimony confirmed the general impression of most surgeons that most patients do not understand the safety risk information they view, nor are they able to determine whether they

¹⁴³ See *Marketing or Medicine: Are Direct-to-Consumer Medical Device Ads Playing Doctor?: Hearing before the Senate Special Committee on Aging*, 110th CONGRESS (Sept. 17, 2008) http://www.aging.senate.gov/hearing_detail.cfm?id=303085.

¹⁴⁴ *Hearing before the Senate Special Committee on Aging*, 110th CONGRESS (Sept. 17, 2008) (opening statement of Senator Herb Kohl).

¹⁴⁵ *Marketing or Medicine: Are Direct-to-Consumer Medical Device Ads Playing Doctor?: Hearing Before the Senate Special Committee on Aging*, 110th CONGRESS (Sept. 17, 2008) (Statement by Stephen J. Ubl, President and CEO of the Advanced Medical Technology Association, Advamed) http://www.aging.senate.gov/hearing_detail.cfm?id=303085.

are suitable candidates for the device.¹⁴⁶ Again, there is no data to suggest that understanding genetics and predictive biostatistics is any easier for consumers to understand than information on implantable medical devices.

One of the physicians who testified was the first speaker to point out, in a congressional hearing, the entrepreneurial relationship physicians are more likely to have with medical device manufacturers compared to pharmaceutical companies and the role of medical device technology in hospital and surgical group marketing efforts.¹⁴⁷ The same fear of financial conflicts of interest for academic physicians who have developed potentially highly lucrative medical devices applies equally to personalized genetic testing kits, as recent Baylor College of Medicine experience seems to demonstrate.

D. The Next Steps Towards More FDA Regulation

The FDA has, within the past few years, issued a series of guidance documents¹⁴⁸ for industry on the increasingly complex genetic testing kit technology. Additionally, the FDA has proposed a series of rules that began to address the FDA's long-standing, and apparently inadequate, discretionary enforcement policy exempting "home-brew" laboratory tests from direct FDA regulation.¹⁴⁹

¹⁴⁶ *Marketing or Medicine: Are Direct-to-Consumer Medical Device Ads Playing Doctor?: Hearing Before the Senate Special Committee on Aging*, 110th CONGRESS 4-7 (Sept. 17, 2008) [hereafter Bozie statement] (Statement of Kevin J. Bozic, M.D., M.B.A.), http://www.aging.senate.gov/hearing_detail.cfm?id=303085. "A ten percent decrease in the number of revision hip and knee arthroplasties in 2005 would have saved the Centers for Medicare and Medicaid Services (CMS) over \$100 million that year." *Id.* at 8.

¹⁴⁷ *Id.* at 2-4.

¹⁴⁸ U.S. FOOD AND DRUG ADMINISTRATION, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, GUIDANCE FOR INDUSTRY AND FDA STAFF - In Vitro Diagnostic (IVD) Device Studies - Frequently Asked Questions, Draft Guidance Oct. 25, 2007, <http://www.fda.gov/cdrh/oivd/guidance/1587.html>.

¹⁴⁹ Although ASRs are medical devices, the FDA has done little to regulate them and no final rule has ever been published in the Federal Register. See generally THE NATIONAL HUMAN GENOME RESEARCH INSTITUTE, RESPONSE OF THE TASK FORCE TO THE FOOD AND DRUG ADMINISTRATION'S PROPOSED RULE ON ANALYTE SPECIFIC REAGENTS APPENDIX 2 (1997), on LSU LAW CENTER'S MEDICAL AND PUBLIC HEALTH LAW SITE, <http://biotech.law.lsu.edu/research/fed/tfgt/appendix2.htm> (last visited Mar. 15, 2009).

Although issuing guidance documents has become the FDA's favorite mechanism¹⁵⁰ for signaling to industry its current thinking and regulatory direction, and for avoiding the administrative law matrix involved in the formal notice and comment rulemaking approach, the proposed rules and guidance documents are problematic because they are non-binding.

Real regulatory control will take effect only when final rules are issued, and the FDA should do so. As previously mentioned, legislation¹⁵¹ was introduced by Senators Kennedy and Obama in 2007 which would have given the FDA expanded authority over the entire home-brew genetic testing industry. Such legislation should be reintroduced and passed during the current session of Congress. Perhaps the passing of the torch from the "free-market" inanity of the outgoing Bush administration to the "smart regulation" model of the new Obama administration will be the political push the FDA needs to once again fulfill its mission by protecting the U.S. public from questionable quality control, unproven claims, and unbridled commercial exploitation of consumers.

¹⁵⁰ "Starting about 1970, FDA's regulatory approach changed. Faced with increasingly complex substantive issues and a growing number of firms making regulated products, FDA turned toward rulemaking as the principal technique for defining legal requirements. The agency attempted to resolve most of the major issues it confronted through administrative, rather than court, action. The Federal Register thus became the primary vehicle for official resolution of food and drug problems...More recently, FDA has increasingly relied on the promulgation of informal guidance, particularly with respect to pharmaceutical products." HUTT CASEBOOK, *supra* note 16, at viii.

¹⁵¹ S. 736, 110th Cong. §1-9 (2007), "Laboratory Test Improvement Act."