Personal Genomics Follows Pathway to Corner Drugstore; Is Regulation Next?

by Dan Vorhaus

The direct-to-consumer (DTC) genetic testing marketplace is on the move again. Just last week, in Mapping the Personal Genomics Landscape, I wrote that “predicting precisely which consumer services will be offered and how, if at all, they will be regulated, is impossible. All we know is that personal genomics consumers ten years from now are certain to have many, many more options than they do today.”

Turns out we only needed to wait a week – not a decade – for the landscape to shift again. Earlier today, DTC provider Pathway Genomics announced that it was partnering with drugstore giant Walgreens to offer its genetic testing service through most of that chain’s 7,500 stores.

Is Walgreens the Tipping Point for Personal Genomics Regulation? At first blush, this might appear to be nothing more than a creative product partnership between a fledgling personal genomics company and a giant drugstore chain. As it turns out, there are early indications that the Pathway/Walgreens partnership could turn out to be a tipping point in the regulation of personal genomics.

With that in mind, and since this post is slightly longer than usual, here’s a quick roadmap for the remainder of this article:


II. Location, Location, Location. Why this time it is the location of the product that matters, and not its price or its content.

III. Enter the Gatekeepers. Though this is not the first time concerns have been voiced about DTC genetic testing, the direct comments from an FDA official are particularly striking, and suggest that these concerns may be finally be ready to produce a regulatory response.

IV. The Regulation of DTC Genetic Testing. This section, and its two sub-sections: The FDA and LDTs and CLIA, Validity and Utility, provide a detailed but still high-level overview of the core components of federal genetic testing regulation, particularly as it pertains to DTC genetic testing. These sections are lengthy, and if you’re not interested in the nuts and bolts of genetic testing regulation you should feel free to skim or skip them.

V. Enforcement Discretion. An examination of the FDA’s decision to voluntarily refrain from regulating most genetic tests, and an overview of proposed regulations that would expand the FDA’s activities in this area.

VI. The Open Secret of DTC Medical Genetic Testing. A review of how certain DTC genetic testing companies attempt to distinguish between the provision of genetic information and medical genetic testing, and why that distinction is proving increasingly difficult to maintain.

VII. Coulda, Woulda, Shoulda. As established earlier, it is likely that the FDA could regulate DTC genetic tests more aggressively. This final section asks whether (a) the Pathway/Walgreens partnership will cause the FDA to exercise its dormant regulatory authority and (b) whether it should do so.

Aisle 8: Spit Kits. The details of the new Pathway/Walgreens partnership are slightly more complicated than walking into the drug store and walking out with a report summarizing your genetic variation. What Pathway is actually selling in the store is an Insight™ Saliva Collection Kit (or “spit kit,” as it is more colloquially known), which will retail for $20 to $30. That's all that you can actually pull off of the shelf and carry out of the store.

The actual genetic analysis occurs only once the customer mails the spit kit to Pathway and heads online to purchase a specific service, at an additional fee. Those fees range from $79 (drug response) to $179 (either carrier testing or health and disease testing) all the way up to $249 for all three testing services in one package. (Interestingly, there is no information in the Pathway press release about the cost of obtaining Pathway’s Ancestry Report using the Walgreens pricing model.) Factoring in the cost of the spit kit, the total cost to the consumer looks to be, at most, $279 for Pathway’s full service. That would make it $150 cheaper than Pathway’s primary DTC competitor, 23andMe, whose similar product retails online for $429.

Location, Location, Location. Typically, newsworthy developments in consumer personal genomics relate to either the content or price of the service, along with periodic pieces reviewing the dire condition of the industry as a whole. This time, however, it is all about location. The fact that a genetic test (or, to be more precise, a saliva collection device that is a requisite first step in obtaining a genetic test) will be offered directly to consumers in a brick and mortar drugstore, and not exclusively online, is a development that is drawing an unexpected amount of attention. (Several publications, including GenomeWeb, have pointed out that this is not the first time a genetic test has been sold by a drugstore, although it is certainly the most widespread such collaboration.)

While most of the coverage of the Pathway announcement has been straightforward and fact-oriented, The Washington Post is one publication that sees this as a much bigger deal.

The over-the-counter test marks the first foray of personalized genomic medicine into the corner drugstore. The move is being welcomed by those who hope that deciphering the genetic code will launch a new era in biomedical science. But it's being feared by those who worry it will open a Pandora's box of confusion, privacy violations, genetic discrimination and other issues.

The Post goes on to quote respected Stanford University bioethicist Hank Greely, who calls the decision to offer Pathway’s tests directly in...
stores “reckless,” and Genetic Alliance director Sharon Terry, who doesn’t believe the test is “something people should be spending their money on yet.”

Of course, not everyone agrees that the migration of spit kits from websites to Walgreens is a Big Deal. Misha Angrist, in Chapter 38 of the Sky Is Falling, suggests that the “only substantive difference in this case is that instead of going online, [consumers] go to the drugstore and possibly burn a few calories in the process.”

Mary Carmichael of Newsweek also wonders why The Post is so concerned by the Walgreens development. Carmichael theorizes that the worry is not “about this particular test, per se, but about the savvy way it’s being sold.” As has been well-documented, the market for DTC genetic tests is fairly small, particularly for tests focused on health and disease (as opposed to ancestry), such as several of the services offered by Pathway.

One likely reason for the failure of DTC genetic testing to reach large numbers of customers is that, for all of its advantages, online commerce takes place in a vast and unruly marketplace where it can be hard for new products to stand out, no matter how creative their advertising. By comparison, even the largest Walgreens is quite manageable, and Carmichael rightly points out that by appearing on the shelves of thousands of Walgreens across the country:

Pathway’s DTC genomic test will be the first one to reach a wide variety of people – including some who won’t have a lot of knowledge about genetics and who may not know how much stock to put in their test results. That’s what [The Washington Post, et al.] are so worried about.

The overriding concern voiced by those critical of the Pathway/Walgreens announcement, as Carmichael aptly notes, is that individuals will not be capable of understanding and acting on the results of a genetic test without professional guidance.

Enter the Gatekeepers. That concern is not surprising, nor is it new. Whether individuals are capable of handling their own genetic information is a question that has attached itself to personal genomics since the outset (and one which The Post covered in some detail earlier this year). The debate has extended beyond consumer personal genomics to genomic research as well.

Not everybody is convinced that this is a real issue at this point. Misha Angrist sees

the panicked response to [the Pathway/Walgreens announcement] from doctors and academics as elitist: it assumes that the ordinary person is stupid and/or not entitled to his or her genetic information without a third-party ‘expert.’ Let’s be real: that ship sailed in 2007. (emphasis added)

While Angrist correctly points out that DTC genetic tests have been available since 2007 (Pathway’s test, which launched in 2009, was predated by similar offerings from 23andMe, deCODEme and Navigenics), this is one ship that just might be towed back into port.

For all of the rhetoric in The Post and elsewhere, here is the one comment that is truly newsworthy:

They are making medical claims. We don’t know whether the test works and whether patients are taking actions that could put them in jeopardy based on the test.

So said Alberto Gutierrez, Director of the FDA’s Office of In Vitro Diagnostic Device Evaluation and Safety, which makes it more than just another commentator’s opinion. Commentators’ concerns about the dangers of DTC genetic testing services are backed, they hope, by the force of evidence and reason. Regulators’ concerns, on the other hand, are backed by the force of civil and criminal penalties authorized by legislatures. As if to drive home that point, Gutierrez added “we think this would be an illegally marketed device if [Pathway Genomics], was 1, in “(pdf) that stands as the most comprehensive resource available to date. On the whole, the regulatory landscape for genetic testing providers shows considerable variation based on the nature of the test (e.g., disease testing vs. ancestry testing), the location at which the test is conducted (both the geographical and the regulatory status of the facility performing the test) and the nature (e.g., physician vs. patient vs. consumer) and geographical location of the individual ordering the test.

The Regulation of DTC Genetic Testing. Understanding the possibilities for increased regulation of genetic testing requires a review of the fairly complex current regulatory framework. Part of the complexity is in determining why and how certain types of genetic tests, including DTC genetic tests, are not presently regulated.

The Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) provides the best background resource in this area. The SACGHS advises the Secretary of the Department of Health and Human Services (DHHS), the umbrella agency that includes the FDA, CMS and the NIH, “on the broad range of human health and societal issues raised by the development and use and potential misuse of genetic technologies.” In that advisory capacity, in April of 2008 the SACGHS produced a 276-page report on “The U.S. System of Oversight of Genetic Testing” (pdf) that stands as the most comprehensive resource available to date. On the whole, the regulatory landscape for genetic testing providers shows considerable variation based on the nature of the test (e.g., disease testing vs. ancestry testing), the location at which the test is conducted (both the geographical and the regulatory status of the facility performing the test) and the nature (e.g., physician vs. patient vs. consumer) and geographical location of the individual ordering the test.

The FDA and LDTs. As it pertains to DTC genetic testing companies specifically, the most salient feature of the SACGHS report was likely the reminder that the FDA, which is tasked with interpreting and enforcing the Federal Food, Drug, and Cosmetic Act (FFDCA), has repeatedly asserted that it has the authority to regulate genetic tests, pursuant to its authority to regulate medical devices under the FFDCA. 1 While some have questioned in the past whether the FDA actually has jurisdiction over genetic tests (pdf), any attempt to forestall increased regulation by
attacking FDA jurisdiction is probably a dead letter given the strong statutory presumption in favor of FDA jurisdiction.\textsuperscript{\textcopyright}

At present, whether a genetic test is subject to FDA regulation largely depends on how it is developed and marketed. The literature, as well as current FDA regulatory policy, divides genetic tests into two primary categories:

(i) in vitro diagnostic test kits\textsuperscript{4} (also sometimes referred to as IVD kits or, simply, as genetic test kits), which may be sold by their manufacturers directly to consumers, testing laboratories, clinicians or other approved recipients, depending on the device; and

(ii) laboratory developed tests (or LDTs, also sometimes referred to as “home brew” assays), which are not sold directly to the general public or to physicians; rather, a testing service (as opposed to the actual test itself) is marketed, and samples (e.g., of saliva) are collected and submitted to the laboratory for evaluation.

The FDA regulates IVD kits as medical devices subject to FDA’s standard medical device regulatory regime, which involves an inquiry into both the analytical and clinical performance of regulated devices.\textsuperscript{3}

However, the majority of current genetic tests – and almost all new DTC genetic tests – are developed as LDTs and are much more lightly regulated. Currently, LDTs are subject to the FDA regulatory scheme that applies to medical devices (including IVD kits) only if they contain FDA-registered analytic specific reagents (ASRs).\textsuperscript{5} Most ASRs are Class I devices under the FDA’s regulations, and therefore subject only to general controls, not to premarket approval or other special controls. However, when tests are regulated as Class I devices they must include a disclaimer stating that the test has not been approved or cleared by the FDA.

While the regulatory status of specific DTC genetic tests is unclear, and depends on the precise nature of the test and the service through which it is provided, at least one firm has adopted language consistent with Class I language. 23andMe, for instance, offers the following disclaimer:

The genotyping services of 23andMe are performed in LabCorp’s CLIA-certified laboratory. The tests have not been cleared or approved by the FDA but have been analytically validated according to CLIA standards. The information on this page is intended for research and educational purposes only, and is not for diagnostic use.

That does not mean that 23andMe necessarily considers itself to be providing a regulated medical device, and despite some diligent searching, I’ve been unable to locate a similar disclaimer on Pathway’s website (although my inability to locate such a disclaimer does not guarantee its absence). Pathway’s chief science officer, David Becker, did tell The Post today that it was the company’s understanding that “under the current regulation…this test does not have to have FDA approval per se…and we do not claim that is [sic] does.”

As is typical of the regulatory framework for genetic testing, the current regulatory status of DTC genetic tests remains unclear. What is clear, however, is that, at least for the moment and in most cases, regulatory oversight from the FDA is fairly minimal.

**CLIA, Validity and Utility.** The FDA’s reluctance to regulate LDTs, particularly of the DTC variety, does not mean that these tests go entirely unregulated. In addition to a variety of state regulations, there are other sources of federal regulatory authority.

The most well-known of these is the Clinical Laboratory Improvement Amendments of 1988, or CLIA, which is enforced by the Centers for Medicare & Medicaid Services (CMS). Labs that perform human testing, including genetic testing, are regulated through a CLIA certification process. For a lab to obtain CLIA certification, it must satisfy CMS requirements relating to quality control, personnel qualifications, records maintenance, and proficiency testing.

CLIA certification also requires the laboratory to demonstrate the analytical validity of its tests,\textsuperscript{6} although it makes no inquiry into tests’ clinical validity.\textsuperscript{7} That is, while CLIA certification addresses whether a lab’s tests perform consistently and control variation to the extent possible (analytical validity), there is no agency inquiry into the tests’ accuracy in detecting the presence of a given condition or phenotype or predicting the development of a disease (clinical validity). Nor does CLIA certification involve an assessment of the clinical utility of a test, an inquiry which involves comparing the benefits of a test to its associated costs and harms. Establishing the clinical utility of DTC genetic testing has been a source of particular contention.

For the moment, all reputable DTC genetic testing providers appear to be conducting their tests in CLIA certified environments. In practice, this works as follows: the consumer purchases a spit kit (either online or, as of this week, at the drugstore), fills it with saliva, then sends it to the DTC company for testing. The actual genetic testing may be performed directly by the company itself (Pathway, for example, operates its own CLIA facility), or by an outside genetic testing laboratory (23andMe, for example, outsources its testing to LabCorp, which operates its own CLIA facility).

The net result is that most DTC genetic tests are subject to some degree of regulation with respect to analytical validity. Unlike IVD kits, however, few if any DTC genetic tests are subject to federal regulatory oversight with respect to clinical validity or clinical utility.

**Enforcement Discretion.** When it comes to the FDA, LDTs and the regulation of DTC genetic testing, about the only thing that’s truly clear is that the FDA appears to have substantially more regulatory authority than it is currently exercising. Despite this authority, the FDA has, for several years now, utilized “enforcement discretion” with respect to the vast majority of LDTs.

Late last year, Don St. Pierre, deputy director of the FDA’s Office of In Vitro Diagnostic Device Evaluation and Safety, the same office Alberto Gutierrez now heads, described the agency’s thinking on LDTs in stark terms:

If a lab makes an LDT, then it is a medical device manufacturer. Just because you have a CLIA certificate does not mean you are not a...
medical device maker, and everything you do is under FDA enforcement discretion.

To put it another way, just because the FDA has been largely content to sit on the sidelines and watch the genetic testing industry proliferate, there is no guarantee that it will continue to do so.

And the FDA has certainly made regulatory overtures in the past. In July of 2007 the FDA published draft guidance outlining its proposed regulatory approach to a specific type of LDT: in vitro diagnostic multivariate index assays (IVDMIAs). An IVDMIA is a device that:

(1) combines the values of multiple variables using an interpretation function to yield a single, patient-specific result (e.g. a “classification,” “score,” “index,” etc.) that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, and

(2) provides a result whose derivation is non-transparent and cannot be independently derived or verified by the end user.

An example of an IVDMIA that has already been cleared by the FDA is MammaPrint, a test for predicting whether an existing cancer will metastasize in women with early-stage breast cancer.

Final IVDMIA regulations have not been issued, but in January another FDA official from the In Vitro Diagnostics office, Elizabeth Mansfield, told Tuma Ray of GenomeWeb’s Pharmacogenomics Reporter that the “IVDMIA guidance is still on the table.” Added Mansfield, “We want to see what we need to do. Do we need to do anything? How much do we need to do? Who do we need to look at? Who don’t we need to look at?”

The Open Secret of DTC Medical Genetic Testing. Mansfield’s comments illustrate the uncertainty over whether any new FDA regulatory initiative will necessarily include the current set of DTC genetic tests, including all or some of those offered by Pathway Genomics, 23andMe and others.

The definition of IVDMIA proposed in the FDA’s draft guidance included those tests that are “…intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease….” If new regulations should arrive, will the definition look substantially the same? More importantly, will the FDA categorize any or all of the current DTC genetic tests as being intended for medical diagnosis, treatment or prevention?

Six months ago, in “The Open Secret of DTC Medical Genetic Testing,” I wrote that the continued expansion of DTC genetic testing services had strengthened the immediacy of the relationship between genetic testing and medical treatment decisions, which clearly relates to the FDA’s supervisory mandate under the FFDCA. Nothing in the past six months has changed that analysis. Indeed, it has become increasingly clear that many DTC genetic testing services are aimed at guiding clinical or medical decision-making, including the selection of therapeutics (e.g., pharmacogenetics testing) and the decision to reproduce (e.g., carrier screening).

For the moment, 23andMe, Pathway Genomics and other DTC genetic testing companies continue in their attempts to navigate a razor-thin divide between clinical and consumer personal genomics. The website materials for 23andMe’s “Health Edition” product, for instance, invite consumers to “take a more active role in managing your health” by learning of genetic risks for “various diseases and conditions [that] will allow you and your doctor to focus on the lifestyle changes and preventative steps that matter most for you.” 23andMe’s terms of service, however, tell a different story, in large boldface type:

23andMe Service Is For Research and Educational Use Only. We Do Not Provide Medical Advice, And The Services Cannot Be Used For Health Ascertainment or Disease Purposes.

Pathway Genomics presents a similar case. The description of Pathway’s Health Kit product promises consumers access to genetic information and guidance that will “allow you to modify your health regime so that you may live a healthier, longer life” and “empowers you and your doctor to make decisions that could save your life.” The terms of service, on the other hand, state that “Pathway Genomics and the Services do not provide medical advice or diagnosis or treatment recommendations for diseases or other health conditions.”

There may well be a narrow but real divide between the act of supplying consumers with genetic information of possible medical relevance and the act of providing direct medical advice and diagnoses. However, looking at the product materials offered by DTC genetic testing companies, it is increasingly difficult to believe that the average consumer – whether shopping online, or in line at Walgreens – will be capable of parsing such a fine distinction. When it comes to mapping the future of the personal genomics landscape, however, the more important question is whether that distinction will continue to hold water with regulatory agencies.

Coulida, Woulda, Shoulda. Last fall, when I wrote about The Open Secret of DTC Medical Genetic Testing, I took pains to note that the fact that these companies could be regulated by the FDA and other agencies, by extending the existing legal and regulatory framework, did not necessarily mean that they should or would be regulated.

As for the would, the statement from the FDA’s Gutierrez, that Pathway would be guilty of offering “an illegally marketed device if it proceeds with its Walgreens partnership, is the clearest signal yet that the FDA may have decided it has been long enough on the sidelines. While that’s not a promise that the FDA will abandon its enforcement discretion, it is the strongest hint the FDA has given to date that it would be prepared to undertake direct regulatory action against a DTC genetic testing company.

One of the questions posed in Five Questions for Personal Genomics in 2010 was whether this would be the year that the FDA, in coordination with CMS, finally tackles the approval and regulation of diagnostic tests through the development of a premarket approval process, a nationwide test registry or some other means? “We’re less than five months into 2010 and the NIH has already announced its plans...
Now it appears that the next regulatory development may be the implementation of a more robust premarket approval process for genetic tests, including DTC genetic tests. Neither of these developments should come as complete surprises.

The response from both industry and regulators in the coming weeks and months will bear watching. My guess is that any new regulations will be implemented gradually, and may not impact all of the products offered by DTC companies, including Pathway and 23andMe.

When Pathway Genomics launched last summer, I applauded the company’s decision to separate its ancestry product from its other health and disease products by using separate customized SNP chips:

...Pathway’s launch reflects a new wrinkle in how the industry may attempt to respond to the anticipated regulation of clinical genetic testing. Differentiating its recreational and clinical products from the outset could be just the sort of subtle but significant decision that would allow Pathway to quickly adapt to any regulations that distinguish educational or recreational uses of genetic data (such as genealogy) from clinical or medical uses (such as disease, pharmacogenetics or carrier testing).

23andMe soon followed suit, and the strategy continues to strike me as a well-conceived one. It would not be a surprise to see the first wave of regulations distinguish between tests that return information of clinical significance and those that do not, with the latter continuing to be available directly to consumers with little or no premarket oversight.

Finally, there’s the lingering question of whether the FDA and other regulatory bodies should play a more active role in regulating the genetic testing marketplace, including DTC genetic test providers. Here is what I wrote six months ago:

As for the should, it’s still not clear that, even if they are offering medical genetic testing, companies such as 23andMe are posing a risk to either consumer or patient safety that requires increased regulatory activity. Policy considerations such as the legitimate interest of individuals in obtaining direct access to their genetic information and a desire to foster the growth of an emerging commercial field to speed the development of technology as well as consumer awareness of the benefits of genetic testing are balanced against sincere concerns by clinicians that their patients may be misled or harmed by inaccurate or incomplete genetic information. The scale does not appear to have tipped definitively in either direction.

It will be fascinating to see if Pathway’s partnership with Walgreens, seemingly a stroke of clever product positioning, turns out to be a tipping point in the regulation of personal genomics, particularly DTC genetic tests. The Pathway/Walgreens announcement has not actually increased the availability of DTC genetic tests. They will still be available to any individual (other than residents of New York State, which requires a separate laboratory license that Pathway has not obtained) with an internet connection, functioning salivary glands and some disposable income.

What has changed is their visibility. It is just possible that one of the safest strategies for avoiding regulation - out-of-sight, out-of-mind - played a significant role in the regulation (or lack thereof) of DTC genetic testing. Tests once predominantly available only to early adopters capable of seeking them out online will now begin to appear on the shelves of thousands of neighborhood drugstores nationwide. To a greater degree than ever before, genetic testing will soon be available to mainstream America (and subject to the impulse buy). And that, for better or for worse, may be all that it takes to convince some regulators that the time for action is finally at hand.

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1 62 Fed. Reg. 62, 249 (Nov. 21, 1997) (“FDA believes that laboratories developing [in-house] tests are acting as manufacturers of medical devices and are subject to FDA jurisdiction under the Act.”).

2 21 U.S.C. § 379a (“In any action to enforce the requirements of this chapter respecting a device, food, drug, or cosmetic the connection with interstate commerce required for jurisdiction in such action shall be presumed to exist.”)

3 An in vitro diagnostic test kit is generally understood in the industry to be an in vitro diagnostic product, as set forth in 21 C.F.R. § 809.3 which defines in vitro diagnostic devices as “those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.” Although the word “kit” has no specific regulatory definition, its meaning is generally understood by the FDA and the industry. See e.g., FDA, Guidance on Pharmacogenetic Tests and Genetic Tests for Heritable Markers (June 19, 2007) (use of the word “kit” in agency guidance).

4 See 21 C.F.R. § 860.7(d)(1) (explaining the circumstances under which FDA considers a device safe); 21 C.F.R. § 860.7(2) (explaining the circumstances under which FDA considers a device effective).

5 See 21 C.F.R. § 864.40209(a). ASRs are “antibodies, both polyclonal and monoclonal, specific receptor proteins, ligands, nucleic acid sequences, and similar reagents which, through specific binding or chemical reaction with substances in a specimen, are intended for use in a diagnostic application for identification and quantification of an individual chemical substance or ligand in biological specimens.”

6 As discussed in the SACGHS report, and elsewhere, CLIA has established specific requirements for certain areas of testing, including microbiology and cytogenetics. CMS has not established a specialty under CLIA for genetic testing, despite several past recommendations that it do so (although the SACHGS report did not echo this recommendation).


8 The FDA’s mandate includes protecting the public by ensuring that “there is a reasonable assurance of the safety and effectiveness of