The FDA and DTC Genetic Testing: Setting the Record Straight

by Dan Vorhaus

Earlier this week, I attended a public two-day meeting of the FDA’s Molecular and Clinical Genetics Panel (“MCGP”) in Gaithersburg, MD. The meeting was not particularly well attended (approximately 100 people were in the room) but the topic of the panel’s deliberations - how to appropriately regulate direct-to-consumer (DTC) genetic tests - has sparked intense and ongoing public debate.

Numerous private and public conversations following the meeting indicate that there is considerable confusion about what actually happened at the meeting, including what the MCGP “recommended” to the FDA and what the FDA is likely to do with those recommendations. With that in mind, I followed up today with Dr. Alberto Gutierrez and Dr. Elizabeth Mansfield of the FDA’s Office of In Vitro Diagnostic Evaluation and Safety (OIVD) to seek clarification.

The MCGP’s “Recommendations.” Perhaps the single greatest source of confusion, and concern, centers on the MCGP’s “recommendations” to the FDA. A likely cause of this confusion is the original Federal Register notice (pdf), published last month, which indicated that at this week’s meeting the MCGP would “discuss and make recommendations on scientific issues concerning direct to consumer (DTC) genetic tests that make medical claims,” including the risks and benefits of offering such DTC genetic tests without clinician involvement. It was not immediately clear, even after the first day of the meeting, what form, if any, those recommendations would take.

As it turns out, “recommendations” is simply the wrong word to describe what the MCGP actually provided to the FDA.

The MCGP was formed three years ago (pdf) to advise the FDA on scientific issues relating to molecular and clinical genetics. Gutierrez and Mansfield confirmed that the panel was not formed, nor was its membership adjusted, in contemplation of the DTC meeting. While the panelists are certainly experts in their respective fields, a majority of the panelists did not appear to be well versed in the technologies, products (including specific tests) and business models employed by DTC genetic testing companies.

At the meeting, the MCGP heard presentations from the FDA, invited speakers (my own slides) and other parties who requested an opportunity to speak to the panel, including representatives from several DTC companies. With these presentations providing context, the MCGP then spent several sessions spread over two days commenting on the three primary questions, and numerous subquestions (pdf), on which the FDA sought the panel's input.

Although a number of panelists consistently offered their opinion that the vast majority of genetic tests should be “routed through a physician,” for many questions there was no clear consensus from the MCGP. Furthermore, the panel’s deliberations were largely unstructured and, for most of the questions asked by the FDA, there was time for only a minority of the 21 panelists to offer their input.

Here, then, are a few important points of clarification about the MCGP’s activities at this week's meeting and its influence on the FDA:

- The MCGP did offer its input in response to a number of specific questions (pdf) presented by the FDA;
- The MCGP did not vote or otherwise establish formal consensus with respect to any of those questions;
- The MCGP will not issue written recommendations following the meeting to the FDA with respect to any of those questions; and
- The FDA is not bound by the input it received from the MCGP in determining how to regulate DTC genetic tests moving forward.

With those clarifications in mind, did the MCGP actually accomplish anything of substance during the two day meeting? As I wrote earlier in the week, probably not:

...we should be careful not to inflate the importance of the MCGP’s recommendations. While they will be the most recent, and certainly the most public (by statute, MCGP meetings are open to the public absent a specific reason for closure) DTC recommendations, they will remain but one set of non-binding recommendations among many sets of recommendations, solicited and unsolicited, received by the FDA.

Furthermore, the MCGP’s composition (the panel’s 21 members feature 18 clinicians and academics, one consumer representative, one patient representative and one industry representative) and fairly obvious inexperience with DTC genetic testing technologies, products, companies and issues should diminish the weight the FDA lends to its recommendations. Whatever you may think of the FDA’s DTC policies to date, or lack thereof, the agency has been considering how to regulate DTC genetic tests for years, and is clearly more knowledgeable on this topic than its own advisory panel.

Ultimately, while it’s hard to find fault with the FDA for holding a public meeting on a topic of such public interest, it has been even harder to locate any indication that this meeting, or the MCGP’s recommendations, will significantly alter the agency’s thinking on the topic of clinical DTC genetic testing.

Nothing from day two of the meeting, or subsequent conversations with FDA officials, has suggested any reason to change this analysis. The MCGP’s input will surely be considered by the FDA, but I can find no credible evidence or argument to suggest that its “recommendations,” such as they were, will have a material impact on the manner in which FDA decides to proceed with the regulation of DTC genetic tests.

What’s Next for DTC Genetic Testing Regulation? For nearly a year, the FDA has publicly stated that it considers many genetic tests currently offered directly to consumers to represent medical devices subject to regulation under Section 201 of the Federal Food, Drug and Cosmetic Act (FDCA). Each of the published “it has come to our attention” letters sent by the FDA to DTC companies in 2010 (first to Pathway Genomics, next to five more companies, including 23andMe, and finally to 14 more companies) clearly made this point. Both Gutierrez and Mansfield reiterated this point at this week’s meeting.
The issue, for quite some time now, has not been whether the FDA intends to regulate DTC genetic tests. Instead, it has been (i) what form that regulation will take and (ii) when and how it will be implemented. Thus, the purpose of this past week’s meeting was not to solicit input on whether to regulate DTC genetic tests - at least for the FDA, that ship appears to have sailed and, as I argued at the meeting, most people agree that some additional oversight of the DTC genetic testing industry would be beneficial - but to discuss how such tests should be regulated, including “the risks and benefits of making clinical genetic tests available for direct access by a consumer without the involvement of a clinician” (pdf).

Again, despite suggestions from many panelists that a clinician should be involved in the ordering and interpretation of the vast majority of genetic tests, there was no formal or binding recommendation to that effect from the MCGP. Nor will one be forthcoming. There is also no good reason to suspect that genetic tests which are currently available DTC without clinician involvement, some of which have remained available for nearly a year since the FDA first publicly announced its intention to regulate these tests as medical devices, are going to be yanked from the market by the FDA tomorrow. If you’re considering purchasing a DTC genetic test, there are plenty of factors to consider in determining whether to take the plunge. A concern that you might not have the option next week should probably not be one of them.

When will the FDA decide to act more aggressively, if at all? That remains unclear. For the moment, the FDA is waiting for formal company submissions to review, while numerous companies, for their part, seek clearer guidance from the FDA regarding what types of products the agency might approve, and what data might need to be collected in order to win an approval. As for the continued availability of DTC genetic tests, some companies (e.g., Pathway Genomics) responded to the FDA’s letters by voluntarily removing their products while they seek to come into compliance. Others (e.g., 23andMe) have continued to offer their products directly to consumers while they negotiate with the FDA. Both companies, as Turna Ray of Pharmacogenetic Reporter writes, are prepared to comply with FDA regulations but ultimately committed to maintaining direct consumer access to DTC genetic tests. While it’s possible that the FDA will move aggressively against currently available DTC genetic tests at some point this year, I have noted, repeatedly, the low probability of this type of significant industry-wide regulation in 2011, and I continue to stand by that prediction.

**Doctor’s Orders?** So just what is the FDA likely to do, and when is it likely to do it? As discussed by FDA officials at the meeting, the FDA plans to continue to work with companies to develop appropriate regulatory submissions (which will be published once reviewed), with formal, public FDA regulatory guidance for DTC genetic tests following only after the agency has been through the clearance process, start-to-finish, with one or more products. While nothing is set in stone, and Congressional action could always upend everything, this is the most likely path forward for DTC genetic testing regulation.

As for what shape the FDA’s regulation will take, should it succeed (and remember, not all attempted FDA regulations ultimately succeed), there are a number of important questions to consider. For example:

- Should the agency require proof of analytical validity, clinical validity and/or clinical utility prior to approving a particular test and, if so, what standards of proof should be required?
- Should the agency regulate tests SNP-by-SNP, claim-by-claim or test-by-test, and what should be done to prepare for the inevitable arrival of tests based on whole-genome sequence data?
- Should the agency oversee the labeling and advertising claims offered by companies in association with such tests?
- Should the agency require companies to collect and submit data regarding the post-test benefits and harms and the actual (as compared to intended) uses of their tests?
- Should the agency impose requirements on companies to prevent unauthorized testing, protect data privacy and limit companies’ ability to share genetic information without their customers’ consent?

While these questions, and countless more, will be critical to the development of sensible genetic testing regulation, one question clearly generates more and more emotional responses than any other:

- Should regulators require some or all genetic tests to be routed through a clinician, or should tests be made available directly to consumers who desire them?

And so we come full circle. It was on exactly this question that the FDA solicited input from the MCGP, as well as other stakeholders, at this past week’s meeting. It was in answering this question that the MCGP developed the clearest consensus. And it is in reaction to this question, and to the comments from MCGP members at the meeting, that many proponents of DTC genetic testing feel most strongly that the FDA is in danger of going badly awry. Many individuals are seriously concerned that the FDA either does not understand or is simply not interested in how the actual and potential purchasers of these tests feel.

Many people believe, as do I, that “people have a right to access their own genetic information.” However, as I have also written and argued on multiple occasions, I do not believe the FDA is seeking to ban individuals’ access to their raw genetic or genomic data. Nothing that has happened this past week has convinced me otherwise. In the unlikely event that I am wrong, and the FDA in due course attempts to broadly restrict individual access to genetic information, there are a variety of factors (including the increasing clinical importance and availability of genetic data, the move to personally controlled medical records, the declining cost of generating genetic data and the globalization of the personal genomics marketplace, to name just a few) that seem certain to frustrate such an effort. Therefore, whatever the short-term consequences of any FDA action in this area, I fully expect that in the not-too-distant-future all individuals who desire it will have ready and inexpensive access to their complete genomic data, whether or not the FDA (or a panel of clinicians or anybody else) thinks that it is a good idea.

**Setting the Record Straight.** But that doesn’t mean that what the FDA does today does not matter, and it doesn’t mean that those who are concerned with how the FDA is seeking to regulate DTC genetic tests should not speak up. While the FDA has been atypically forthcoming in public discussions with details of its plans to regulate DTC genetic testing, the availability of genetic information, and the area of personal genomics more broadly, is one of atypical interest to many members of the public. Clearly, for many, the FDA has not listened closely enough
If you are confused or concerned by the FDA's actions in this area, speak up. Although the FDA does not regulate by majority vote, that happens to be exactly how Congressmen are elected, and one good option is to follow Jennifer Wagner's lead and write a letter to your representatives in Washington.

For those who would prefer to express their views directly to the FDA, while the public DTC meeting has concluded, there will be several additional opportunities to be heard. First, the agency has agreed to reopen the public docket from this past week's meeting to permit the submission of additional public comments into the official record for consideration by the FDA. You can find the docket at regulations.gov, docket number “FDA-2011-N-0066”. In addition, after holding three public “Town Hall” meetings in 2010, CDRH is holding another three meetings this year. The first was held this week, in Irving, Texas, with CDRH Director Jeffrey Shuren and other FDA officials.

Particularly in the context of DTC genetic testing, where so many of the reasons offered for stronger regulation revolve around how people actually react, or might react, to the results of genetic tests, personal experiences and views can be influential in shaping the FDA's policy. Thankfully, there are still plenty of opportunities for the public to set the record straight on how it feels about the FDA's plans to regulate DTC genetic tests.