FDA's Role in the Oversight of Direct-to-Consumer Marketing of Genetic Tests
Deborah Wolf, J.D.

DR. TUCKSON: Let's move now then to Deborah Wolf's presentation. Deborah is going to update us on the FDA's role in the oversight of direct-to-consumer marketing of genetic tests. She is with the Office of Compliance, Center for Devices and Radiological Health at FDA.

Then after Deborah's comments, we'll come back and put all of the pieces together and determine as you listen to what she has to say, and what you heard, how we might move forward in terms of our agenda in this regard.

Deborah, thank you so much.

MS. WOLF: You're welcome. I'm glad to be here. Good morning, everybody.

I want to make a couple of quick points before I start my slides. One is that I would acknowledge that we do work slowly in general. I think in part that's because of the bureaucracy itself and the way that government works in general. Part of it has to do with resources, and part of it has to do with these issues being complicated.

There is not always consist opinion or agreement inside the agency or within the department. These things just require a great deal of discussion before there is really any movement.

The other thing I wanted to say is that my presentation includes a lot of references to specific statutory and regulatory provisions. I hope that you don't find that off putting. I think here a lot of the specific language in the statute and the regs is important. That's why I kind of did it this legalistic way.

Direct-to-consumer marketing of genetic testing is taking place in a much larger context of direct-to-consumer marketing of all kinds of medical products and services. So I think that's one part of how you look at the entire field of consumer reaction, what prompts consumers to have a specific test.

There have been a number of studies done on the impact of different aspects of DTC marketing of drugs, especially. There really are a lot of mixed opinions in the consumer and medical communities.

The advertising and access of genetic testing raised concerns that are different from those of advertising or direct access of drugs and medical devices. Some of them are the same in terms of who is making certain decisions, what kind of guidance they have. But there are also, as we've heard, a lot of much larger consequences.

The FDA's role is uncertain.

In vitro diagnostics provide information rather than treatment. So when the agency approves or clears a diagnostic test, the safety and efficacy are reviewed in a different way, or they are viewed differently from the way that they would be viewed for drugs and devices that are used in therapy. The consequences are sort of one step removed. The test itself generally isn't causing any sort of danger. It is what happens with how good the test is, how reliable it is, and what happens with the information that you glean from it.

These are kind of the basic aspects of promotion and advertising of medical devices that we look at. Pre-market notification and pre-market approval are the two ways that medical devices get to market. The labeling and advertising authority that FDA has over medical devices, intended use has to do with the kinds of claims that company makes for the use of its products. All of this touches the practice of medicine, which FDA doesn't regulate. I'm going to touch on our work with the Federal Trade Commission.

For pre-market notification, these are generally lower risk devices. Essentially these are devices that are cleared for marketing based on being equivalent to a product that either is on the market now or was on the market prior to the date that the Medical Device Amendments were enacted in 1976.

For the most part, general controls and special controls apply to these devices. They don't get the same rigorous review that products that require pre-market approval do. The company submits a pre-market approval application, and the product will be approved if the way that the conditions of use are presented in the labeling provide reasonable assurance that the product, if it is used according to the label, is generally safe and effective.

Central to our regulation of analyte-specific reagents and how that affects genetic testing, an approval order granted to a Class III device that requires pre-market approval. The approval order can restrict the sale or the use and distribution of the device. To the same extent that is permitted by Section 520(e) of the statute which basically says that if FDA believes it is necessary, they can require that the sale, distribution, and use of the device be restricted by regulation so that it is either made into a prescription product or upon any other kinds of conditions that FDA thinks are necessary to provide safety and effectiveness.

520(e) referred to restricting devices through regulation. There are only three devices currently restricted by regulation. Any other restricted devices are restricted through its approval order, and those are all the Class III, more rigorously reviewed devices. The only three that are restricted by regulation are analyte-specific reagents, drug of abuse test kits, and hearing aids. As I said, most restricted devices are Class III that require pre-market approval and they are restricted through their approval order.

Section 502(q) Of the Food, Drug, and Cosmetic Act provides that a restricted device and restricted either by regulation or by approval order, that a restricted device is misbranded if the advertising is false or misleading in any particular or it is sold, distributed, or used in violation of any regs prescribed under Section 520(e).

So for analyte-specific reagents, which are restricted by regulation, 502(q) means that it would be misbranded if the advertising for that ASR is false, misleading, or it is sold in violation of the restrictions captured in the regulations, which I'm going to mention in a minute.

Section 502(r) of the Act provides that that same restricted device is misbranded if the advertising doesn't include a statement of product's intended use, and a summary of relevant risk information.

Device labeling, which is a broad category of material, it includes any sort of handout, a glossy brochure, any piece of material essentially that a company distributes is labeling. A device is misbranded if its labeling is false or misleading in any particular. That applies to all devices, and not only restricted devices. The advertising limitations that I talked about were for only restricted devices, but FDA has labeling authority over all devices.

Labeling, as I said, is interpreted broadly. The material doesn't have to be physically with the product to be considered labeling. As long as it is textually related, it has been determined through case law that essentially if it is about the product, it is labeling.

Advertising is not really defined in the Food, Drug, and Cosmetic Act. It's mentioned, as you saw, but it isn't defined. So the Center for Drug Evaluation and Research has regulations. The way that they define advertisements basically is ads that you think about sort of intuitively as an ad in published journals and magazines, other periodicals and broadcast ads.

Our review of advertising as opposed to labeling brings us closely into working with the Federal Trade Commission. In 1971, there was a memorandum of understanding between the two agencies that essentially decided that FDA would have primary jurisdiction over the advertising of prescription drugs and of restricted devices, those devices restricted by approval order or by regulation, and over the labeling of all products.

The Federal Trade Commission has primary jurisdiction over advertising of other than restricted devices, and of over-the-counter drugs.

One thing that's very important in terms of the genetic testing issue is that FDA hasn't really clearly defined the Internet as either labeling or advertising. So while we do apply our jurisdiction, it is not clear for the most part whether we are actually defining it as labeling or advertising. In the substance of the claim that we look at, we did have an Internet working group a number of years ago that was attempting to make that determination. That group was disbanded.

The Federal Trade Commission has a broader authority over advertising in general which is why their role is very important in this area.

Analyte-specific reagents used in IVD testing are restricted, as I said, by regulation under the authority of 520(e). This is the regulation that I have shown here, 21 CFR 809.30, which restricts the sale of ASRs. They can be sold to IVD manufacturers, they can be sold to labs that are regulated under CLIA and granted high complexity determination, and then they can be sold to organizations that use the reagents for other than medical diagnostic purposes.

The labeling for ASRs is limited as well. The labeling has to make clear that analytical and performance characteristics are not established. For Class II and Class III, products get a higher review analyte-specific reagent, except as a component of a specific test, analytical and performance characteristics are not established.

The reason that's important is that when the tests are marketed and they are marketed only to labs, they are not allowed to make a claim for the intended use of the ASR. Once they do that, it becomes a device subject to FDA's jurisdiction.

The advertising, the regs on ASRs require that the advertising and promotion,
which includes their labeling and their advertising, include the identity of the analyte, and again, the limitations. For Class II and Class III, as I said, they're limited to whatever tests they may have been shown to be used for.

Class II and Class III are higher risk uses essentially. Class II are mostly blood bank kinds of analytes, and Class III are HIV tests and TB tests, and a number of others.

This is also in the regs. Ordering in-house tests developed using analyte-specific reagents is limited under Section 520(e) of the Act, the restriction, to physicians and other persons authorized by applicable state law to order such tests, unless, as I said, it is sold to IVD manufacturers or organizations using it for other than medical diagnostic purposes.

So what happens here is that in all of this direct marketing to consumers, the tests that are used in labs, the home-brew tests that are developed using the analyte-specific reagents are technically limited by regulation. No one should be ordering the tests except physicians.

You do have the way that a lot of medical device, contact lenses, and a lot of prescription drugs, a lot of the websites that sell those will have a physician on their staff who is perfectly willing to write you a prescription. Whether that's valid, the prescription itself in that setting where you have no relationship with the physician, depends mostly on state law. So the states regulate pharmacy and the boards of medicine. So who can actually prescribe a test is up to the states.

This would be helpful in terms of our regulation of tests used, developed by labs using ASRs if we knew how to apply this, and if there were support in the agency to support it. It's not clear here actually whether this would restrict the lab from accepting an order.

The problem here is it doesn't really discuss who comes under the jurisdiction, and who would be responsible for basically not ordering in-house tests.

So the question is this genetic testing involving home brew and laboratory developed testing is really whether the combination of the ASR, which we do regulate, and the lab process, become a device. Whether the conjunction of those two things become a device, and how would we limit the ordering of those things to physicians, first establishing whether it is a device, and then, as I said, this issue of Internet prescribers.

Limiting access to the tests, even if we could enforce that part of the regulations, wouldn't prevent labs from advertising the tests. A question is whether advertising a specific use for an ASR by the lab creates a device that requires pre-market approval.

Generally what starts FDA's jurisdiction over the product is the claim that a company is making for it. So if a lab is establishing a use, then they could misbrand the device if that were an inappropriate claim for the ASR.

When we look at enforcement as a whole, and with specific reference to IVDs and tests, FDA is focusing right now on risk-based reviews, both in terms of public health priorities and in terms of resources. Here for ASRs and laboratory tests, there are a lot of issues about whether the tests are valid, whether they have been shown to provide the information that they claim to provide, look at the consequences of false negative or false positive results with these tests, as several of you have talked about. The kinds of decisions, health care decisions that people will make, or employment decisions, or all sorts of things that may result from an incorrect answer.

We would look at the seriousness of the disease or condition, the role of genetic counseling, and then the issue about whether genetic information places a certain burden on people that they may not want. All of these things are broader issues that FDA really can't decide itself, but that go into our calculus.

The agency has cleared about 12 genetic test kits. These last three are among the more recent. Dr. Joe Hackett, who is here, can speak more specifically about these tests if anybody has specific questions. I'm not a scientist, I don't really know what exactly they do.

Then these are some of the kinds of claims that we are worried about. As Matt said, we need a slam dunk. There are a lot of claims out there, but in trying to identify, here we talked about the impact of wrong information or the seriousness of the disease. We need to put all of those together when we're looking at how to best use resources.

So these are the ones that we have identified, as Matt said, a chart with a number of Internet companies. These are the kinds of claims that we've sent for now. Companies have claimed that their test can predict how someone will metabolize drugs or have adverse drug reactions, nutritional counseling, tendencies toward obesity, and detecting susceptibility to serious kinds of conditions. Cardiac disease, cancers, bone mineral density, and risk for osteoporosis, autoimmune diseases, chronic fatigue, and a number of infectious diseases.

As we have said, FDA and FTC are working now together to coordinate some of the information we've collected, the information on websites. I want to sort of point out that right now we're focused on Internet websites. There are other kinds of advertising for these products. I haven't actually seen a lot of it. The use of the Internet has become so widespread, and it's national. This is a good place for us to start.

Thank you.

DR. TUCKSON: Thank you very much, and also the other comments that were made by Matt and Muin as well.

Why don't you take a seat, because I know we'll have a lot of questions and it would probably be easier to take them from your seat.