



## Days Before Warfarin Label Change, Genelex Debuts DTC Dosing Dx; ASHG's 'Validity' Notice Could Help

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**Genelex**, the direct-to-consumer genetic testing shop, rolled out a warfarin dosing product earlier this month, three days before US regulators and Bristol-Myers Squibb added a black box warning to the label of the ubiquitous anticoagulant, marketed by BMS under the trade name Coumadin.

Genelex's test also comes on the scene as the American Society for Human Genetics prepares to release a statement that declares "there is nothing inherently bad about DTC testing," and that aims to help define which DTC testing shops produce clinically valid data [[see related story, this issue](#)].

As a result, Seattle-based Genelex, a tiny shop with 17 staffers, is betting that its DTC product will succeed where Roche's AmpliChip continues to struggle: Selling drug-metabolism tests.

### Grassroots

Genelex has been selling DTC tests since 2000 and provides paternity tests, DNA-based forensics, genealogy services, and pharmacogenomic services based on CYP2D6, 2CP, 2C19, 1A2, and NAT2. Its tests are based on Tm Biosciences' Tag-It platform.

The new warfarin test interrogates 2C9 and the VKORC1 gene, which helps determine how much warfarin needs to be in the body for the drug to have a clinical effect. Patients order the test through the company's web site or by telephone, receive a buccal swab kit and instructions, and return their sample to Genelex.

Genelex uses an algorithm to crunch the patient's 2C9 and VKORC1 genotype along with age and height information and returns the results, including dosing recommendations, four or five days later.

Coleman said this information "allows you to predict a maintenance dose of warfarin to within 1 milligram to 1.5-milligrams per day."

The test, which has its own CPT code, costs \$550 and Coleman said some payors "routinely reimburse" for it.

It's estimated that between 300,000 and 500,000 new patients are prescribed warfarin each year, and that between 2 million and 5 million are on it at any one time. Based on these figures, Genelex could be facing a \$2.8-billion market.

Coleman conceded that “there’s really no market” for these kinds of tests at the moment, but stressed that companies like Genelex, Roche, and Clinical Data, which released its own PGx-based warfarin test last week (see [PGx Reporter 10/11/06](#)), are “just at the start of a growth curve.”

To help scale the curve, Genelex has launched a grassroots marketing campaign, also aimed at patients, which includes giving talks at anticoagulant clinics and direct mail. In this way Genelex is not exclusively DTC, but Coleman said efforts to win over anticoag clinics are another way to get physicians’ attention.

“One of our goals with this service is to bring the physicians into the fold” of pharmacogenomics, Coleman told *Pharmacogenomics Reporter* this week.

“We believe people have a right to their genomic information, and we believe people have a right to control access to it,” he said. He said this privacy risks being lost if tests are ordered for patients by health organizations. “Their genetic information is going to wind up in their medical records, and in this case it’s not really theirs.”

According to Coleman, Genelex keeps “most records and DNA” for at least five years in a “secure facility.” He said the company does this “for quality and regulatory purposes,” and said “it’s also a convenience for clients who may need a copy of their report or file or want additional testing performed.”

However, he stressed that “under no circumstances do we release records to third parties without express written instructions from the client. If the records were to be subpoenaed, we notify the client of the subpoena and will not release the records without their permission or a court order,” Coleman said.

He claims that “old records are shredded and old DNA is bleached and sewerred.”

### **‘No Market ... Now’**

Coleman readily admits that the Genelex warfarin test will be playing in a market that has yet to emerge. Roche, the world’s biggest molecular diagnostic company and the leading edge of a movement to use CYP450 genotypes to learn how individuals metabolize drugs, has so far been losing its bet with its AmpliChip test, which, despite being an FDA-approved IVD and backed by an army of salespeople and marketers, has failed to catch on [see [PGx Reporter 9/6/2006](#)].

The AmpliChip CYP450 test identifies CYP2D6 and CYP2C19 genotypes, and Roche markets it as a broad metabolism assay, rather than a test specifically for warfarin dosage.

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Coleman said his primary competitors are CLIA high-complexity labs and other reference labs, but stressed that these labs are passive test suppliers that react to physicians’ prescriptions. By comparison, Genelex, by marketing its tests to patients, bypasses physicians who may not be knowledgeable about pharmacogenomics while indirectly making them a part of the process.

Coleman said Genelex plans to release a coag panel that includes clotting tests such as Factor V Leiden. The firm is also considering using its service in the psychiatric market.

Moreover, companies selling gene-based warfarin dosing tests could get a leg up in the market if the FDA fulfills its promise to change warfarin’s label to reflect the ability of certain genotypes to affect the way the drug is metabolized.

Larry Lesko, director of the FDA Office of Clinical Pharmacology and Biopharmaceuticals at the FDA's Center for Drug Evaluation and Research, in June 2005 said an updated warfarin label "would have to" include information about polymorphisms of both CYP450 2C9 and VKORC1, "because either one alone doesn't make for a persuasive label change [see [PGx Reporter 6/16/2005](#)]."

Last week's label change for warfarin added a new patient medication guide and highlighted current safety information in a black box warning. While the new label includes information about the role patient metabolism plays in warfarin response, it does not make any genetic dosing recommendations.

### Passing Muster

Gelenex is taking a seat at a table that includes patient advocacy groups, physicians, regulators, and legislators who claim that DTC genetic tests can be difficult to understand at best and useless or harmful at worst.

But Coleman said "there seems to be quite a different attitude" about DTC tests today than there was, say, three years ago when he was "taken to task" by a panel on which he was participating.

In fact, the ASHG unveiled a policy statement about DTC testing earlier this month at its annual conference in New Orleans. The statement, which is set to appear on the group's web site this week, says that companies wishing to sell DTC tests must, for example, be CLIA labs, they need to be transparent about what they are doing, and they must have a privacy policy.

Coleman said Genelex complies with all of the ASHG suggestions, which will be open for public comment once they are posted on the web site.

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Gail Javitt, law and policy director at the Genetics and Public Policy Center, said "from a consumer's perspective, given the current regulatory environment, it's really not possible to know which tests have so-called 'clinical validity' and which ones don't."

This is where the ASHG's policy statement comes in. Joanne Boughman, executive vice president of ASHG, said the statement is meant to "affirm that there is nothing inherently bad about DTC testing, and that in the absence of federal regulatory requirements — as

we are right now — that transparency on the part of the provider of the test is essential."

Javitt, who is also a Research Scientist in the Berman Bioethics Institute at Johns Hopkins University, agrees with the ASHG in that "there needs to be more transparency that when someone offers a test [they need to show] what data they have to support their claims."

But she said what the DTC genetic testing market really needs is a genetics testing specialty under CLIA [see [PGx Reporter 8/2/2006](#) and [9/27/2006](#)].

Compounding the issue further is a policy statement released in 2004 by the American College of Medical Genetics, the ASHG offshoot. That one-paragraph note, which Javitt said "takes a fairly negative stance toward DTC" tests, said that genetic tests are "medical tests" and "should be provided to the public only through the services of an appropriately qualified health care professional."

The ACMG goes on to say that “due to the complexities of genetic testing and counseling, the self-ordering of genetic tests by patients over the telephone or the Internet, and their use of genetic ‘home testing’ kits, is potentially harmful.”

An ACMG spokesperson said the 2-year-old note, which can be found [here](#), continues to represent the group’s policy on DTC genetic testing. She added that the group plans to look more carefully at the DTC genetic testing issue in 2007.