

# Pharmacogenomics Reporter

March 5, 2008

## Hayes Debuts Gene Test-Evaluation Service To Help Payors Determine Validity of Tests

**AT A TIME WHEN PAYORS** are increasingly demanding that diagnostic tests be clinically useful and valid in order to garner reimbursement, Philadelphia-based healthcare research and analysis firm Hayes has launched a service designed to help insurers, hospitals, and policymakers sift through the published data to make this determination.

“As these tests come to the forefront of diagnosis and treatment of disease, there are many questions regarding their accuracy, validity, and clinical utility,” said Winifred Hayes, CEO of the company. Hayes’ Genetic Test Evaluation Service “provides a clear, objective view of the science behind these tests, the hard clinical evidence supporting them, and the use of the tests in clinical practice.”

In a statement announcing the launch of the service last month, Hayes claims GTE is the “first evidence-based service to address these issues through application of the Hayes Rating,” which she said is a proprietary test-grading system “that is a standard in the industry.”

For instance, a test that receives an “A” is found by Hayes to have “Established Benefit,” or good evidence suggesting it has validity and utility. On the other end of the scale, if a test gets a “D” then the test has “No Proven Benefit,” meaning it lacks validity or utility, or there is insufficient evidence to evaluate the test.

The grade is determined based on the data Hayes gathers from at least three studies published in scientific journals,

including a validation study conducted independently of the company manufacturing the test, and a clinical validity study. The studies have to “clearly establish the association between the genetic makeup of the population and the physical presentation of the disease, or the phenotype-genotype association,” Diane Allingham-Hawkins, GTE director, told *Pharmacogenomics Reporter*.

The service is subscription-based, online, and uses a framework developed through the CDC’s National Office of Public Health Genomics to determine if a test has analytical and clinical validity, and if it is clinically useful. The CDC’s *ACCE framework* puts forth a series of questions about the analytic validity, clinical validity, clinical utility, and ethical, legal, and social implications of the test. The grade given by Hayes is determined based on the answers it can gather from published data.

The analytical validity looks at a test’s sensitivity or its ability to detect certain genetic mutations; its specificity, which ensures that it tests for the disease it claims to; and issues of quality control and the robustness of the assay. Under the ACCE framework, Hayes looks at the specificity and sensitivity of the test at a clinical level, the prevalence of the disorder in the population, and the positive predictive value of the assay. The service also tries to assess the clinical utility of the test, or what the genetic test will mean to patient care.

In assessing the clinical utility of a test, Hayes tries to answer the questions: “Just because we can do it, should we do it? Does the test add anything at all?” posited Allingham-Hawkins.

“There are lots of tests out there that don’t really add any benefit. It doesn’t really change anything in the care of the patient other than cost,” she said. “So you have the same information you would have had, except you have it in a different way.”

In fact, an analysis by Hayes’ experts gave low marks to some widely used genetic tests. According to Hayes, several breast cancer recurrence tests, continued on next page



[www.genomeweb.com](http://www.genomeweb.com)  
The GenomeWeb Intelligence Network

© 2008 GenomeWeb, LLC. All rights reserved. Copying, photocopying or duplicating this publication in any form other than as permitted by agreement with GenomeWeb, LLC is prohibited and may constitute copyright infringement subject to liability up to \$100,000 per infringement. For photocopy permission, back issues, bulk distribution or site licenses, please contact Greg Anderson at +1.212.651.5632 or ganderson@genomeweb.com.

March 5, 2008

including Agendia's FDA-approved MammaPrint, Genomic Health's Oncotype DX, and Veridex's Rotterdam Signature — all of which are reimbursed by some payors — all received a Hayes Ratings of “C” or lower.

The clinical utility portion of the service is becoming a major concern for payors as the health care system transitions from one-size-fits-all to a more personalized paradigm, as scientists make advancements in pharmacogenomics knowledge, and with the introduction of over a thousand genetic tests into the market in the last few years.

For instance, although there are several marketed genetic tests for identifying patients at risk for developing serious adverse events when treated with the widely used anticoagulant warfarin, there has been debate among academics and policy makers as to the clinical utility of these tests after a highly publicized [clinical trial](#) on pharmacogenomics-guided warfarin dosing did not reach its primary endpoint [see [PGx Reporter 12-05-2007](#)].

“Millions of dollars are being spent on genetic tests by hospitals and insurers, and by consumers,” Hayes said in a statement. “But our initial analysis [of the market] indicates that the evidence is insufficient to substantiate the clinical validity and utility of many of these tests, despite their increasing use.”

Hayes' analysis contradicts Genomic Health's experience with Oncotype DX. According to company officials, since the firm launched the test in 2004, patient adoption has increased, fueled by the company's success in garnering reimbursement with national and local insurers.

Health plans that together cover 70 percent of US lives now reimburse for Oncotype DX. Additionally, as a result of the company publishing studies about Oncotype DX clinical utility and validity in peer-reviewed journals, Oncotype DX was recently included in the American Society of Clinical Oncology and the National Comprehensive Cancer Network's treatment guidelines for patients with early-stage breast cancer [see [PGx Reporter 02-06-2008](#)].

Other diagnostic test developers have not had such a positive experience establishing the clinical utility and validity

of their tests with payors. Roche officials have spoken out against insurance companies having too stringent coverage requirements for genetic tests by holding them to the same evidence standards as drugs and other medical products [see [PGx Reporter 04-25-2007](#)].

Aetna is one of the insurers that has decided not to cover Roche Diagnostics' FDA-approved AmpliChip. While Aetna has in many ways embraced personalized medicine—by instating comprehensive program of coverage policies, providing physician education, and enacting privacy provisions around BRCA

testing for inherited breast and ovarian cancer—the insurer also demands high evidence standards when determining which genetic tests to cover. The insurer claims that Roche's test has yet to meet the evidence requirements for reimbursement.

According to Aetna, among these requirements is the need for Roche to perform controlled clinical trials to prove that the AmpliChip will reduce adverse drug reactions. Aetna also has asked that Roche to compare the test, which interrogates CYP2D6 and CYP2C19 polymorphisms, with standard therapeutic

drug-monitoring techniques.

Another piece addressed by Hayes' GTE service is the social and ethical implications surrounding genetic tests. Doctors worry about malpractice suits as diagnostic companies market genetic tests to a population that largely does not understand the science, and into a healthcare system ill-prepared to handle the social and ethical concerns the science raises.

For instance, legal experts often describe the growing prevalence of so-called “wrongful birth” lawsuits in which parents sue healthcare professionals for failing to adequately inform them of the risk of a genetic abnormality in an unborn child [see [PGx Reporter 10-10-2007](#)].

Hayes characterizes the ethical issues surrounding a test by using the CDC's ACCE framework, which puts forth several questions exploring the types of stigmatization, discrimination, privacy/confidentiality and personal/family issues the test raises; the legal issues regarding consent, ownership of data

---

*“Millions of dollars are being spent on genetic tests by hospitals and insurers, and by consumers. But our initial analysis indicates that the evidence is insufficient to substantiate the clinical validity and utility of many of these tests, despite their increasing use.”*

---

March 5, 2008

and/or samples, patents, licensing, proprietary testing, obligation to disclose, or reporting requirements; and the safeguards in place to thwart ethical abuses.

“Many of these tests suggest a correlation to disease, which could unnecessarily cause concern among patients who may never develop the disease,” Hayes said in a statement. “In other cases, there may be no way to prevent or treat the disease, and it’s unclear how the test result can be used to improve patient management. It’s essential that these tests be

used only when there is evidence that there will be some benefit to the patient.”

According to Hayes, its research products and advisory services are used by more than 65 percent of US healthcare insurers serving approximately 150 million lives, hospitals making health technology-acquisition decisions, and employers helping staff make better healthcare choices.

*by Turna Ray*