FDA soon may support biomarker tests

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The Food and Drug Administration is poised to throw its support behind a powerful new method of predicting the safety of experimental drugs, a step that could help pharmaceutical companies bring treatments to market more quickly - and reduce patients' risk.

The process being considered uses seven indicators - known as biomarkers - that signal kidney injury when found in the urine of test subjects.

"Today, the FDA gives approval for a new drug or device, but there has previously been no way to obtain approval for a new and better way to test a drug for its safety," said Raymond Woosley, president and CEO of the nonprofit Critical Path Institute, which is working with the FDA to safely speed drug development.

Currently, experimental drugs are tested in animals before being taken to human clinical trails. But animals' reactions aren't always the best predictor of whether substances will be safe for humans. Drugs harmless to animals can hurt humans, and vice versa. If a drug toxic to the kidneys passes animal tests today, the damage might not show up until it is too late.

"Using current tests, you have lost about 70 percent of the kidney function before you pick it up," says William Mattes, director of toxicology at the Critical Path Institute in Tucson.

The new biomarker process has the potential to save a patient's kidneys.

The ultimate goal of the pharmaceutical industry is to have a range of such marker tests that would signal dangerous side effects like heart failure, liver damage or cancer. Samples of blood, urine or saliva, for example, would be taken from participants in a clinical trial. If certain biomarkers indicated the patient was at risk, the trial could be stopped before any major damage occurs.

Seventeen companies have joined the research into biomarkers at the Critical Path Institute. These include giants like Bristol-Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Merck and Co. and Pfizer. The companies contribute their expertise but, according to Woosley, the institute does not accept commercial funding.

Initially, the seven biomarker testing processes will be qualified by the FDA for use in preclinical animal studies, and only as a complement to current tests.

"This qualification process allows the industry to have an accurate view of the application of these biomarkers in drug development. They are not replacing anything that is done today. But the goal, as we gather more and more information, is to eventually be able to include them in clinical trials," said Federico Goodsaid, senior staff scientist at the genomics group at the FDA Office of Clinical Pharmacology.

Goodsaid is responsible for the development of the FDA's biomarker qualification pilot process, which began about a year ago when 23 potential biomarkers for kidney damage were submitted to the federal agency. The evaluation process at the Critical Path Institute has since selected the seven most efficient ones.

Named for the risky period when a drug is taken from the preclinical stage into clinical trials, the Critical Path Institute was founded two years ago by the FDA in collaboration with University of Arizona and Menlo Park's SRI International to break a worrying trend within the pharmaceutical industry: In the past decade the number of innovative therapies submitted for FDA approval dropped by 50 percent, but the cost of drug development increased dramatically.

Meanwhile, scares like the one associated with the painkiller Vioxx, which turned out to cause heart attacks and strokes, have further fueled this trend.

Unique for the Critical Path Institute is that FDA is a cofounder. Today, the European Medicines Agency - an agency similar to the FDA - also participates as an adviser. The agency is expected to qualify the seven biomarker testing method simultaneously with FDA.

"This is the first time they have coordinated their decisions," Mattes said.

Sidney Wolfe, director of the health research group at Public Citizen, a nonprofit public interest organization, supports the use of biomarkers as long as they are properly validated. But he is critical of the FDA's attitude toward present drug safety tests.

"Findings of toxicity in the currently required animal tests are not taken seriously enough by companies or by the FDA," Wolfe said.

He cites two recent examples of drugs in trouble, both of which showed toxicity in laboratory animals: the diabetes drug Avandia from GlaxoSmithKline and Vytorin from Schering-Plough and Merck, a cholesterol-lowering medication.

"Avandia showed evidence of heart damage in animal studies and, for Vytorin, tests showed serious toxicity in laboratory animals, regardless of how low a dose of this combination drug was used," says Wolfe.

The official announcement of the qualification of the seven biomarkers for kidney injury is expected from the FDA any day.

"It is in a very advanced stage of that process," Goodsaid said. "We should have some news soon."

What are biomarkers?

A biomarker is an indicator that can be used to test a biological function. Some biomarkers turn up when organs are injured and cells within the damaged tissue release substances into the blood, urine or saliva. These substances can then be used to detect dangerous side effects.

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