

FDA Considering Biomarkers As a Way to Improve Drug Safety

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A new way of testing experimental drugs is being considered by the Food & Drug Administration (FDA). If adopted, the FDA could end up requiring "biomarker" tests for all new drugs. Proponents of the new biomarker process say it would help bring new drugs to market more quickly, while at the same time, reduce the risk that patients might be exposed to dangerous side effects that aren't apparent when new drugs are tested in animals. However, some patient advocates, while favoring the adoption of biomarker tests, say they will only be useful if drug makers take their results seriously. In the past, several high profile drugs - for example Avandia and Vytorin - showed signs of toxicity in animal tests. But those problems were ignored and the drugs proceeded to human clinical trials, and were eventually approved by the FDA.

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 be used to detect dangerous side effects. Right now, the FDA is considering a testing process that uses seven indicators - known as biomarkers - that signal kidney injury when found in the urine of test subjects. 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. But ultimately, the pharmaceutical industry would like to see the FDA adopt a range of such biomarker tests for human clinical trials that would signal dangerous side effects like heart failure, liver damage or cancer.

Under current testing protocols, experimental drugs are subjected to animal testing before they can move on to human clinical trials. But animal tests aren't always the best predictor of whether substances will be safe for humans. For example, if a drug toxic to the kidneys passes animal tests today, the damage might not show up until it is too late. Under a biomarker protocol, samples of blood, urine or saliva, 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.

It is hoped that biomarkers will speed the development of new drugs. Over the past 10 years, the number of new drugs and therapies submitted for FDA approval dropped by 50 percent. The move towards biomarkers has also been spurred by safety scandals surrounding some drugs, such as Vioxx, which was found to put users at risk for heart attacks and strokes after it came on the market.

While many patient advocates agree that biomarkers could go a long way towards improving drug safety, they contend the process will only work if drug makers abide by results. And some are skeptical that this will always be the case. Dr. Sidney Wolf of the group Public Citizen told the "San Francisco Chronicle" that in the past, drug makers have ignored safety issues apparent in early testing of drugs. "Findings of toxicity in the currently required animal tests are not taken seriously enough by companies or by the FDA," Wolfe said. "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." Both drugs came under fire in the last year

because of problems, and the companies that developed them have been accused of withholding or downplaying vital information on safety and effectiveness when they were submitted to the FDA for approval.

Unfortunately, it is not unusual for drug makers to use the control they have over drug clinical trials to downplay disturbing findings. Yesterday, two reports in the "Journal of the American Medical Association" (JAMA) found Merck Inc. concealed mortality risks in two key Vioxx studies, and hired "ghostwriters" to author research that was supposedly conducted by independent scientists. Such practices are used throughout the drug industry, though they are hard to document, the authors of the JAMA reports said. Considering this history, it is fair to question whether or not the pharmaceutical companies would attempt to manipulate biomarker tests in the same way.