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Fixing the Drug Laws

THE PHARMACEUTICAL BUSINESS IS A MULTINATIONAL ENTERPRISE OF GREAT SIGNIFICANCE to human health. The U.S. Food and Drug Administration (FDA), once called the world standard in regulating new drug approvals, may still deserve that status. But, as was described earlier in this space, public confidence in the agency has been shaken. That's why it's important that we restore the FDA's capacity to do the quality of work that all health care systems require.

The immediate opportunity to fix things up lies with Congress. A bill authored by Senator Edward Kennedy has passed the Senate. Last month, three former FDA commissioners (myself included) testified before Rep. Henry Waxman's House Oversight Committee and called for stronger budget support, noted problems with the "user fees" mandated by earlier legislation, and cited the growing rate of antibiotic resistance. We also pleaded for improved monitoring of the safety of marketed drugs, already a troubling source of public concern.

With respect to the last of these, the problem is that the United States lacks a system that is adequately tuned to detect adverse reactions. That measure requires a numerator and a denominator: the number of reported adverse events divided by the number of prescriptions issued. The FDA knows neither. Event reporting is voluntary, yielding a record of dubious reliability, and there's no national prescription record. That's why the FDA had to use Kaiser, a large health maintenance organization, to find an adequate database for evaluating the safety of Vioxx.

Information about all clinical trials reviewed by the FDA should be made publicly available at the FDA's Web site and also be linked to the National Institutes of Health's Web site, ClinicalTrials.gov. Why? Recently, a Cleveland Clinic cardiologist analyzed trials conducted on GlaxoSmithKline's diabetic drug Avandia. His meta-analysis revealed cardiovascular risks that had been hinted at in earlier published trials but were not statistically significant in any one trial. The study, published in the *New England Journal of Medicine*, illustrates the difficulty of finding important trial data. The journal has since been attacked by the company, some physicians, and an unfortunate editorial in the *Lancet*, but it deserves praise instead.

On antibiotic resistance, a new report from Resources for the Future (RFF) entitled "Extending the Cure" lays out the contemporary hazards. Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci are widespread in hospitals. The RFF authors note that deaths from the 1918 influenza epidemic were largely from untreated infections—a chilling prospect as we await possible repetition of such an epidemic. The new legislation should provide positive incentives for drug companies to develop new antibiotics, but physicians also need to recognize that their own prescribing behavior exacts external costs on the health care system.

Merely applying policy fixes for these deficiencies can't solve the biggest FDA problem. It's about resources. Consider: In 2003, the first fiscal year after 9/11, the FDA's budget benefited from the Department of Homeland Security. That year's budget would have grown to $1.924 billion in 2007, had it received annual increases of 5.8% to meet the real costs of inflation. Instead, what the FDA actually got was $1.558 billion, 20% below the agency's needs. In its next budget, the FDA needs $2 billion in appropriated funds even to stay level with 2003.

The 1997 legislation mandating user fees got the agency more money, but generated public doubt about the FDA's relationship with industry. The House could pay more attention than the Senate to another problem: User fees can be applied only to the drug approval process, where the new appointments exact costs from the rest of the FDA. Not only are those fees unavailable for drug safety monitoring, they can't be applied to food safety either (think of *Escherichia coli* in spinach and tainted meat).

Beyond addressing the FDA's funding deficit through appropriations rather than user fees, the House should make "orphan drug" provisions clearly available for developers of new drugs that confront antibiotic resistance. Its bill should be firm about requiring public availability of all clinical trial results and include muscular provisions for monitoring drug safety, such as a national database that contains required reports of adverse drug reactions and provisions for a national prescription audit. The latter may be politically naïve, but why take essential needs off the table because they may not be politically popular?

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