40. Food and Drug Administration

The federal government should

- allow market-based certification of the safety and efficacy of initial uses of new drugs and medical devices, just as markets certify the efficacy of subsequent uses; and
- restore individuals' freedom to use any non-FDA-approved product.

Under current law, the Food and Drug Administration must approve all pharmaceuticals and medical devices before they can be marketed. Although the process is often termed ''FDA testing,'' that agency does little if any actual testing. The developer of a new drug uses its own labs or hires another private company to conduct animal tests on the drug for safety before proceeding to clinical trials for safety and efficacy in people. A medical school or a consulting firm often conducts those tests. When each phase of the testing is completed, the pharmaceutical company submits the details of the testing process, evidence of adherence to FDA protocols, and the test results to the FDA.

FDA officials review the test results at each step, and if they are satisfied, they give the pharmaceutical company permission to proceed to the next step in the testing process. When all the tests and trials are complete, FDA officials review all the information—often measured in hundreds of pounds or linear feet of reports rather than number of pages—and decide whether the company can market the drug and advertise it to physicians for the treatment of specific diseases and conditions. The FDA exercises very strict authority over what manufacturers can say about their products. In particular, manufacturers can only promote uses of the product that have been approved by the FDA.

As an agency, the FDA has strong incentives to delay the time when new products reach patients. If the FDA approves a product, it runs the

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risk of patients being harmed, which would lead to criticism of the agency. If the FDA delays approval or requires more tests, the same number of patients (or more) may be harmed by not having access to a beneficial product, but the FDA does not come under criticism because its role is unseen. As Dr. Henry Miller explained:

> In the early 1980s, when I headed the team at the FDA that was reviewing the [new drug application] for recombinant human insulin, the first drug made with gene-splicing techniques, we were ready to recommend approval a mere four months after the application was submitted (at a time when the average time for NDA review was more than two and a half years). . . . [M]y supervisor refused to sign off on the approval—even though he agreed that the data provided compelling evidence of the drug's safety and effectiveness. ''If anything goes wrong,'' he argued, ''think how bad it will look that we approved the drug so quickly.'' . . . The supervisor was more concerned with not looking bad in case of an unforeseen mishap than with getting an important new product to patients who needed it.

The bias toward delay can be readily observed. From 1977 to 1995 the number of clinical trials required to bring a new drug to market doubled and the number of patients involved in those trials nearly tripled. It now takes up to 15 years to complete the FDA-regulated development, testing, and review processes. Joseph DiMasi, Ronald Hansen, and Henry Grabowski estimate that the cost of bringing a new drug to patients has doubled since 1987, to more than $800 million in 2003, while a new drug discovered in 2003 would cost $1.9 billion to bring to patients 12 years hence.

The Human Cost of FDA Delays

Certainly, it is desirable to make all products as safe as possible. But every day that the FDA delays approving a product, many patients who might be helped suffer or die needlessly. Dr. Louis Lasagna, former director of Tufts University's Center for the Study of Drug Development, estimated that the seven-year delay in the approval of beta-blockers as heart medication cost the lives of as many as 119,000 Americans. During the three and a half years it took the FDA to approve the drug Interleukin-2, 25,000 Americans died of kidney cancer even though the drug had already been approved for use in nine other countries. Eugene Schoenfeld, a cancer survivor and president of the National Kidney Cancer Association, maintains that ''IL-2 is one of the worst examples of FDA regulation known to man.'' Patients also suffer needlessly when the FDA causes drugs never to be developed. Researchers have estimated that FDA regulation cut

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by 60 percent the number of new drugs introduced in the 1960s and 1970s. Prof. Christopher Conover of Duke University has estimated that the increased morbidity and mortality due to FDA regulation imposed a net economic cost of $42 billion in 2002 alone.

In the past few decades, patients' groups have become more vocal in demanding timely access to new medication. AIDS sufferers led the way. The Internet allows patients to organize, exchange information, and take more control of their treatment. Patients can track the progress of possible treatments as they are tested for safety and efficacy and are quite conscious of how the FDA can stand in the way of their health and even their survival. In 2003 the Abigail Alliance for Better Access to Developmental Drugs brought suit against the FDA to expand access to unapproved drugs for terminally ill patients with no other hope. After all, if an individual is expected to live for only six months, another year of testing does that person no good.

From FDA Certification to Market-Based Certification

It is past time for Congress to break the FDA monopoly on initial safety and efficacy certification and restore the right of individuals to control their own health care. A model for reform already exists in the private sector.

The United States already has an essentially free-market process for certifying drug efficacy. Even though the FDA approves a drug for one particular use, which goes on the drug's label, physicians may—and do—prescribe drugs for other uses. Examples include

- aspirin, designed for pain relief, which turns out to be effective in preventing heart attacks, and
- Viagra, intended as a treatment for angina, which turns out to be a remedy for erectile dysfunction and has been used to treat pulmonary hypertension, even in premature babies.

Lack of FDA certification does not mean such uses are dangerous or unproven: these so-called ''off-label'' uses are suggested or discovered by doctors and scientists, tested, discussed worldwide in medical journals and symposia, and (if validated) appear in medical textbooks, the *U.S. Pharmacopeia Drug Information*, the *American Hospital Formulary Service Drug Information*, and other authoritative sources. In fact, off-label uses often become the standard of care, particularly in fighting cancer and other diseases. Doctors so frequently rely on market-based certification

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(which arguably includes foreign governments' certifications) that more than half of known drug uses are off-label uses.

Market-based certification respects the freedom of doctors and patients to make treatment decisions according to individual circumstances. It is also more efficient than government certification; one researcher found that off-label uses that were later certified by the FDA were certified by the market (in the *U.S. Pharmacopeia Drug Information*) an average of 2.5 years sooner.

The federal government should build on that success and allow companies to seek initial certification of their products from such market organizations. Those organizations would certify *new* drugs for new uses, just as they now certify *existing* drugs for new uses. They would design and execute the laboratory tests and human studies appropriate for evaluating the safety and efficacy of personalized drugs. To survive, market organizations would have to be scrupulously honest: just as Underwriters Laboratories and *Consumer Reports* sell their reputations, the *U.S. Pharmacopeia* or other organizations would sell their reputations and lose customers if their reputations came into question. Market-based certification and restoring patients' freedom to use any non-FDA-approved product would help Americans capture the benefits of future pharmaceutical innovations, including individually tailored drugs, that the current FDA certification process is likely to suppress.

Some manufacturers will oppose liberalization. Larger companies especially are used to doing business with the FDA. They are comfortable with the confidence the public has in the FDA, and they may view regulations as costs that they can absorb but that their smaller competitors cannot. Such attitudes are even more reason to allow market-based certification.

In a free society, individuals should be free to care for their physical well-being as they see fit, which includes the freedom to choose the medical treatments they think best. Such liberty does not open the door for fraud or abuse any more than does a free market in other products. In fact, informed consent by patients will become more sophisticated as the market for information about medical treatments becomes more free and open.

Suggested Readings

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