43. The Food and Drug Administration

Congress should

- modify the Food, Drug and Cosmetics Act of 1938 to allow pharmaceutical companies to opt out of Food and Drug Administration testing requirements and to use alternative organizations to certify product safety and efficacy and
- allow individuals the 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 an FDA testing program, that agency does little if any actual testing. For example, 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. These tests often are conducted by a medical school department or a consulting firm. 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. Interestingly, over half of product uses are so-called off-label uses as physicians discover that products approved to counter one ailment can be

helpful in preventing or treating other problems. For example, aspirin designed for pain relief turns out to be effective in preventing heart attacks.

As many as 10 years may be necessary to complete the development, testing, and approval process. Some estimates suggest that the cost of bringing a new product from conception to market is on average $400 million. According to the Office of Technology Assessment, the cost of bringing a new pharmaceutical to market is so great that most companies will begin the process only if the market for the drug is expected to be greater than $100 million a year. As a result, companies focus on drugs expected to be "blockbusters," which can be used by essentially everyone with a particular disease in the expectation that the drug will ameliorate or cure it with a marginal risk of causing adverse side effects.

In response to complaints about constantly increasing delays in the drug approval process, the federal government devised a method by which pharmaceutical manufacturers pay FDA to hire and retain additional drug application reviewers. The additional funding may have reduced the time needed for some phases of the approval process. In other words, the FDA imposes a testing burden on pharmaceutical companies; requires that all tests be certified only by the FDA, with no allowance for alternative certification; and then charges the manufacturers to perform the service. Thus the FDA has become a fee-for-service as well as a tax-supported agency.

The Human Costs of FDA Delays

As an agency, the FDA has a strong incentive to delay allowing products to reach the market. After all, if a product that helps millions of individuals causes adverse reactions or even death for a few, the FDA will be subject to adverse publicity, with critics asking why more tests were not conducted. Certainly, it is desirable to make all pharmaceutical products as safe as possible. But for every day that the FDA delays approving a product for market, many patients who might be helped suffer or die needlessly.

For example, Dr. Louis Lasagna, director of Tufts University's Center for the Study of Drug Development, estimates 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." In 1985 the National Heart, Lung and Blood Institute of the National Institutes of Health stopped a study comparing a genetically engineered clot-busting drug called TPa because the study showed that TPa was so effective in reducing heart attack–related deaths that it would be unethical to withhold it from volunteer patients. Yet it took the FDA four more years to approve the drug, despite the NIH decision. That delay cost 30,000 lives.

The FDA often is driven by sensationalist press stories—indeed, the agency often fuels such stories. Consider the example of defibrillators—devices used to revive patients whose hearts have stopped. In the early 1990s scare stories in the press alleged that those devices were malfunctioning and killing patients. Yet after seven years and some 7 million uses, there had been only 630 reported "failures" of defibrillators, about half of which were caused by operator error or other factors not related to the devices. (These devices are often used at the scenes of accidents or fires under difficult conditions that increase the likelihood of mistakes being made.) And "failures" generally did not mean that the devices had delivered shocks that killed the patients; after all, their hearts had already stopped beating. And in some cases the devices simply had to be recharged. Even though the defibrillators functioned correctly in 99.995 percent of cases, pressure from the FDA forced the manufacturer to stop production for years.

In the past decade patients' groups have become more vocal in demanding timely access to new medication. AIDS sufferers led the way. After all, if an individual is expected to live for only two more years, three more years spent testing the efficacy of a prospective treatment does that person no good. The advent of the Internet has allowed individuals suffering from specific ailments and patient groups to use Web sites and chat rooms to exchange information and to actively participate in and take more control of their own treatment. They can track the progress of possible treatments as they are tested for safety and efficacy and are quite conscious of how FDA-imposed delays can stand in the way of their good health and even their lives.

FDA Power Grabs

The FDA often uses its power and censorship authority in a bizarre and irresponsible manner, seemingly exercising it merely because it can and because, as an institution, it wants to expand its power. For example, the FDA proposed classifying a home testing kit for the HIV virus as a

Class 3 medical device—the class that includes heart valves and like devices. The kit essentially consisted of a cup for holding a urine specimen that would be sent to a lab. That attempt was shot down by a U.S. court of appeals.

The FDA ignored the court's implicit warning and soon announced its intention to classify an envelope used for mailing hair samples to a lab for drug testing as a medical device. When the company providing the envelopes challenged the FDA in court, the agency backed off.

Moreover, the FDA's initial objections to a home testing kit for drugs sought not to guarantee the safety and efficacy of the product but to promote the FDA's social agenda—the FDA claimed the kit might cause "family discord." After ridicule from both Republicans and Democrats in Congress, the FDA backed off. But the fact that the agency could use its authority to certify a product's efficacy as a means of determining for parents how they should deal with their children's drug use points to the serious nature of the agency's abuse of power.

The FDA has also claimed jurisdiction over outdoor laser light shows and sought to ban them within 20 miles of a Las Vegas airport. Airline pilots have complained that such shows interfere with flying. One would think that would be a problem for the Federal Aviation Administration, but lasers are classified as medical devices. Thus, the FDA argued that even if lasers were not used for medical care, they were still under FDA jurisdiction under the Radiation Control for Health and Safety Act of 1968.

The FDA's desire to control what manufacturers can say about products was on display at the agency's 1996 conference "FDA and the Internet." The FDA bars manufacturers from disseminating truthful information about their products that the FDA has not first approved. The information and communications revolution clearly undermines the FDA's censorship ability. After all, patients and health care providers might have direct access to a manufacturer's information over the Internet. Thus, the FDA's conference dealt explicitly with the need to regulate Web links and chat rooms. Of course, it is easy to post information from other countries, outside the FDA's jurisdiction. Thus, there were present representatives from Britain, France, Switzerland, Brazil, the Netherlands, and the World Health Organization to discuss global censorship.

The FDA has considered classifying "expert systems" computer software as "medical devices" subject to agency censorship. Doctors routinely consult piles of books to piece together the best evaluation of complex symptoms and ailments and to devise the best strategies for treating them.

Needless to say, such a process can be speeded up significantly if the information is on CD-ROM and a physician can search for cross-references at Pentium speeds. Whether the medium is ink on paper or a digitized piece of plastic with a good search engine, government control is not any less an act of censorship.

In 2000 the Clinton administration proposed that any Web site selling prescription pharmaceutical products be registered with and thus controlled by the FDA. Again, free access to information and products undermines the FDA's control of industries.

There has been some progress recently in resisting FDA censorship. For example, now if another government agency makes a health claim about a product that is regulated by the FDA, for example, if the Agriculture Department claims that certain foods can reduce the risk of cancer, then the FDA cannot hold the private party criminally liable for making the same claim. But FDA's pattern of abusing its power and censorship authority is clear. In an information economy the adverse effects of such abuses will be even more pronounced.

Hindering Designer Drugs

Many people know from media reports, personal experiences, or the experiences of friends or loved ones that some drugs that are effective in most patients simply do not work in other people. Although there is less evidence for the reciprocal situation, in which a drug that is ineffective for most people is the ideal treatment for some patients, such situations surely occur. Other drugs that cause no serious adverse effects in the overwhelming majority of patients can cause illness or even death in some individuals. Those differences in response result from individual differences in patients' genetics, biochemistry, physiology, and sensitivities.

Molecular biology—especially the completion of the mapping of the human genome—and improvements in combinational chemistry and computer science are revolutionizing drug development. An article in *The Economist* on July 1, 2000, put it well:

> The coming century should see a plethora of diagnostics and precisely tailored drugs. It should therefore also see two aphorisms favoured by medical practitioners . . . come true. These are that prevention is better than cure, and that you treat the patient, not the disease . . . you can and should personalize the treatment of the patient.

Dr. Craig Venter, the scientist who leap-frogged the government's ponderous procedures to map the human genome, sees a future in which

cures can be customized for individuals on the basis of a DNA chip. An individual's genetic information could be contained on such a chip. That information would enable physicians to predict the disease susceptibility of particular individuals, to counsel them about the best means of prevention, and to know in advance how they will react to new drugs as they are developed. The DNA chips, Venter estimates, will cost between $50 and $100.

Drugs targeted to small patient populations, whether because the drug will work in a few people or because it will avoid side effects that are expected in only a tiny minority of patients, will not generate $100 million a year in sales. Indeed, the ones that will be most valuable to some at-risk populations will have much, much smaller prospective markets. Thus, the regulatory burden on producing such products will have to be held to a minimum. The alternative is that the science will be wasted and the drug will not reach the market.

DNA chips, containing the genetic information that is unique to each individual, will surely be classified as medical devices by the FDA. The problems in medical device approval parallel those described here for drug approval. How soon or, even, whether DNA chips will be available will depend, in part, on the FDA, unless the current law is changed.

Of course, putting an individual's DNA information on a chip raises privacy issues as well. If individuals allow their DNA information to be kept by physicians and laboratories for specific, defined purposes, firm contracts can specify exactly what uses can and cannot be made of the information. If the FDA is involved, the information might be used against the individual's will. This propensity of the federal government was clear in the Clinton administration's medical privacy regulations that were proposed in November 1999. Those regulations would remove the requirement that the federal government secure permission from individuals to use their medical information, allowing the government, not the individual, to make such determinations.

Two things are certain about the future of personalized medicine. First, its realization will require the availability of a wider selection of drugs than is now on the market. And, second, because of its methods for reviewing the effectiveness and safety of drugs for the general population, the FDA is unprepared to evaluate the myriad drug-genome combinations that must be understood for maximum use of the genome information. The FDA defines efficacy in terms of the greatest good for the greatest number, a one-size-fits-all approach that hinders the development of treatments customized for the needs of specific individuals.

So long as the FDA maintains a monopoly on drug approval, the only way to increase the availability of new pharmaceutical products will be to provide the agency with still more funding and a still larger "campuslike" complex than now planned for its offices. It is inevitable, however, that the agency will remain a bottleneck, slowing the advent of new drugs and the use of "old" drugs in new circumstances.

There is no sense of institutional urgency in the FDA to get pharmaceutical products and medical devices to market quickly. It is unreasonable to expect FDA officials to leave their comfortable, well-rutted schedule of meetings and reviews to wrestle with how best to deliver drugs—safe and effective for some people but, perhaps, risky and ineffective for other people—to the medical profession and the public. It is time for Congress to break the FDA's monopoly on drug and medical device approval, and on information dissemination about drugs and devices, and to allow individuals to take better control of their own health care. To this end, two steps are necessary.

Allow Pharmaceutical Companies to Opt Out of FDA Testing Requirements

The Food, Drug and Cosmetics Act of 1938 should be changed to allow drug companies to seek certification of their products from nongovernmental organizations. Those organizations would have an incentive to move quickly to design and execute the laboratory tests and human studies that are appropriate for evaluating the safety and efficacy of personalized drugs. Instead of the FDA's approval being required before drugs are marketed, the nongovernmental organizations would be allowed to certify new drugs for particular uses and new uses of old drugs. Those certification organizations would have incentives to allow products on the market as quickly as possible but also incentives to be as honest as possible in evaluating the safety and efficacy of products. After all, like Underwriters Laboratories or accounting firms, those organizations are selling their reputations, which, if damaged, would cause them to lose their customers.

Different kinds and levels of certification should be allowed, with full disclosure of information on safety and efficacy. For example, a testing organization might class a certain drug as "risky," with the recommendation that it be used only in life-threatening situations when no other therapy is available. Pharmaceutical manufacturers would be permitted to certify their own products if they chose to forgo the use of an independent certification organization. As a compromise with a fully free system of

certification, manufacturers as well as private testing organizations might be required to label their products "Not FDA Approved."

Some pharmaceutical manufacturers might oppose breaking the FDA's monopoly. Larger companies especially are used to doing business with the agency; they are comfortable with the confidence the public has in FDA-approved drugs; and they could see continuing FDA regulations imposing costs that they could absorb but that their smaller competitors could not. Those attitudes are even more reason to allow private certification.

Allow Individuals the Freedom to Use Any Non-FDA-Approved Product

A basic question concerning any individual with an illness or medical problem is, "Whose life is it anyway?" In a free society individuals should be free to take care of their physical well-being as they see fit. The advent of the Internet gives individuals even more access to information about medical products and treatments. Individuals should be allowed to choose the 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 probably will become more sophisticated as the market for information about medical treatments becomes more free and open.

Conclusion

Many details await congressional attention. That attention will be well rewarded when the future of personalized—more efficacious and safer—medicine is realized. To leave the future of personalized medicine to the FDA will mean, at best, long delays. More likely, it will mean that many efforts to bring the best information about pharmaceuticals and human biology to bear on human illness will simply be abandoned. The cost of FDA-like reviews cannot be recouped through marketing of a drug important, even life saving, to a limited number of people. What should be done, then, is to reduce the FDA-imposed costs by allowing private certification of products and consumer choice.

Suggested Readings

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