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RED TAPE FOR THE DYING: THE FOOD & DRUG ADMINISTRATION AND AIDS

INTRODUCTION

As the American death toll from AIDS passes the 30,000 mark, it is increasingly evident that the disease may become the most serious health crisis of the century. The crisis is being aggravated by federal regulations impeding the distribution and use of medications that could alleviate or postpone some of AIDS' worst consequences. It is this which prompts ads in homosexual-oriented newspapers for bootleg versions of medicines legally unavailable in the United States. For the same reason, widely circulated primers offer detailed advice on how to cross the borders into Mexico and Canada to obtain drugs that cannot be prescribed by U.S. physicians. Underground networks of doctors, patients, and information clearinghouses coordinate research that is shunned by the established world of medicine.

These are not the inevitable consequences of a dread new disease; rather, they are evidence of a regulatory dilemma that can be laid squarely at the door of the U.S. Food and Drug Administration (FDA). Recognizing these problems, the President's Commission on AIDS in February stressed the need to speed the availability of experimental AIDS drugs.[1]

Covert Action. The problems of availability, however, cannot be cured simply by "fine-tuning" regulations or selecting new regulators. They are inherent in FDA's powers to approve new drugs and in the statutes specifying and controlling these powers. Something clearly is wrong when a regulatory program aimed at protecting the health of Americans sends thousands of its supposed beneficiaries into covert action to obtain potentially effective drugs. What is needed is fundamental reform of FDA. The agency's power to block new drugs should be eliminated. While FDA should continue to certify drugs that it finds safe and effective, licensed physicians should be allowed, with the patient's informed consent, to prescribe drugs that are not so certified.

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1 *Chairman's Recommendations For Consideration by the Full Presidential Commission*, February 29, 1988, p. 42.

Risk-Benefit Assessment. This would not make high-risk drug treatments freely available. Malpractice laws and other constraints would ensure that physicians prescribed such drugs only in exceptional cases. What would happen is that pioneering drugs would be similar to pioneering surgery, which is not restricted by government but by risk-benefit assessments made by physicians, patients, and insurers.

Such a measure would improve the likelihood of discovering more effective AIDS remedies and offer long-term incentives for pharmaceutical innovation. Most immediately, it would offer a measure of hope to the thousands of AIDS victims for whom the few currently approved therapies hold no promise.

THE APPROVAL PROCESS FOR NEW DRUGS

Federal power to review the safety and efficacy of new drugs developed in two stages. In 1938, the Food, Drug and Cosmetic Act was passed in response to the deaths of over 100 Americans from an untested new sulfa drug. The act established a New Drug Application (NDA) process, under which no new drug could enter interstate commerce unless determined to be safe by FDA, which itself had been created in 1927.[2] FDA's decision of whether a drug was safe was to be made on the basis of data submitted by the manufacturer. This was the procedure until 1962, when widespread fetal deformities in Europe were attributed to thalidomide, a sedative for use during pregnancy.

Power Over Human Testing. In response to the thalidomide catastrophe, the Food, Drug and Cosmetic Act was amended.[3] Ironically, although the thalidomide case raised only questions of safety, the most fundamental change was to require FDA to certify not only the safety, but the effectiveness of new drugs. Thus applicants were required to prove to FDA's satisfaction not just that their drug was safe, but also that it was effective. Without passing both elements of this test procedure, the new drug could not be marketed. Effectiveness was judged on the basis of the manufacturer's claims for the drug. The applicant, as mandated by the new amendments, had to produce "substantial evidence that the drug will have the effect it purports...to have under the conditions of use prescribed, recommended or suggested in the proposed labeling ...."[4]

The 1962 Amendments also granted FDA power over the human testing of new drugs. The human tests necessary to win approval to market a new drug could henceforth be conducted only under conditions approved in advance by FDA under its investigational new drug (IND) procedures. The FDA regulations subsequently issued under these new statutory powers set out in great detail the nature of the data necessary to show safety and efficacy and the procedures for conducting tests to obtain these data. These regulations form the basis of today's FDA approval procedure.

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2 The agency was known as the Food, Drug and Insecticide Administration until 1931.

3 The use of thalidomide in the United States had been prevented by an ongoing FDA investigation.

4 21 U.S.C. sect. 355(d).

There are three phases in human testing, technically known as clinical investigations. Phase 1 tests aim at obtaining basic data on safety, metabolism, and side effects of a proposed drug. Generally, Phase 1 tests are conducted on fewer than 100 subjects, most of them healthy. Phase 2 tests effectiveness and short-term side effects; they are conducted on several hundred patients, split into treatment and control groups. If Phases 1 and 2 are promising, longer Phase 3 studies begin, concentrating on more detailed issues such as optimal dose rates. This phase can involve hundreds or thousands of patients over a period of several years.[5]

Tests Taking 2 to 10 Years. Once an IND has been approved and clinical testing begins, it can be halted if FDA finds that the tests involve unreasonable risks or even if FDA is merely dissatisfied with the test plan. Complete clinical trials for a new drug can take from two to ten years, and can generate over 80,000 pages of data for a single new drug application.

The new powers granted to the FDA in 1962 fundamentally changed the nature of the agency and the drug development process. Conclude University of Rochester Medicine Professors Louis Lasagna and William Wardell: "FDA shifted after 1962 from essentially an evaluator of evidence and research findings at the end of the [research and development] process to an active participant in the process itself." The result, say the authors, was a transfer of "primary decision-making authority in pharmaceuticals from market mechanisms to a centralized regulatory authority."[6] This shift in drug approval procedures sparked an intense debate which began in the early 1970s and continues unabated today.

DRUG LAG: RECOGNIZING WHAT ISN'T THERE

The expansion of FDA power occurred in the name of improving public health and safety, giving the impression that a stronger FDA was contributing to better health. Beginning in the early 1970s, however, evidence began to mount that the new powers may be damaging the nation's health. According to critics, the benefits produced by FDA in eliminating unsafe and ineffective drugs are far outweighed by the harm caused by the new delays in introducing effective new drugs. University of Chicago economist Sam Peltzman, in a 1972 study, found that drug innovation after 1962 had declined by over 50 percent. He attributes this entirely to the effect of the 1962 amendments. The net social loss from the new law, according to Peltzman, was in the range of $250 million to $350 million annually.[7] In today's dollars, the loss of course would be much higher.

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5 21 C.F.R. sect. 312.21.

6 Henry G. Grabowski and John Vernon, *The Regulation of Pharmaceuticals* (Washington, D.C.: American Enterprise Institute, 1983), p.4.

7 Sam Peltzman, *Regulation of Pharmaceutical Innovation* (Washington, D.C.: American Enterprise Institute, 1974).

A Matter of Life and Death. Soon after Peltzman's work Professors Wardell and Lasagna compared drug availability in the U.S. and Britain. For drugs introduced into both countries in the decade after the 1962 amendments, the medical experts found that Britain enjoyed nearly twice as many drug-years of prior availability as the U.S.[8] In addition, Britain had four times as many of what are called exclusively available drugs, those available only in one of the two countries, as the U.S. In such areas as cardiovascular, respiratory, and gastrointestinal medicine, they found that "nearly all the exclusive drugs are available only in Britain, while introductions in the U.S. appear to have come to a halt...."[9] A 1980 study by the federal General Accounting Office (GAO) yielded similar results. Of 14 significant drugs introduced during a 30-month period in the mid-1970s, GAO found that "all but 1 of them were available earlier in other countries."[10]

In pharmaceutical innovation, delay is not merely an issue of inconvenience or expense. It can be, literally, a matter of life and death. Drug regulation was imposed because it appeared that the market was failing to ensure public health and safety. The possibility that a government program might do worse was never considered.

PREVIOUS REFORMS OF THE NEW DRUG APPLICATION PROCESS

Recognizing problems in the drug approval process, both FDA and Congress have introduced some reforms. In 1975, the agency began a "priority review" process to speed approval of important new drugs; in 1978 it set a goal of cutting New Drug Application, or NDA, review time by up to 25 percent. In 1983, Congress enacted the Orphan Drug Act to encourage research on drugs for rare diseases, where patient populations might be too small to attract the necessary private investment. This act offers tax incentives and exclusive marketing rights for seven years. The 1984 Drug Price Competition and Patent Term Restoration Act created an abbreviated NDA process for generic drugs and extended the 17-year life of drug patents to recoup the time lost during drug testing. In addition, in 1985, FDA issued its "NDA Rewrite," a set of new regulations aimed at streamlining the NDA process through such steps as revised applications and a more lenient policy on accepting foreign clinical data.

The agency's most recent response to the AIDS crisis is its "Treatment IND" regulations, issued last May, which allow treatment of desperately ill patients with drugs that are still being investigated.

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8 Drug-years of prior availability measure the time that drugs are available exclusively in one country before they become available in another. For instance, if Britain were to approve two drugs two years before they were approved in the U.S., the total drug-years of prior availability would be four.

9 William Wardell and Louis Lasagna, *Regulation and Drug Development* (Washington, D.C.: American Enterprise Institute, 1975), p. 77.

10 GAO, *FDA Drug Approval — A Lengthy Process That Delays the Availability of Important New Drugs* (1980), p.8.

Effects of the Reforms

The reform results have been unimpressive. The exclusive marketing provisions of the Orphan Drug Act, for example, have spurred fights between competing firms over whose product is entitled to exclusivity. While FDA approved a record number of new drugs in 1985-1986, one recent study points out that this accomplishment was due partly to many NDAs reaching approval in the last quarter of each year, possibly at the expense of the succeeding year's first-quarter approvals.[11] If this is the case, it obviously could boost the agency's record for only a short period. As for the general issue of drug lag, the study concludes that "the current data suggest a continuation of a trend toward a delay between first foreign marketing and U.S. approval of many new drugs."[12]

The treatment IND regulations represent perhaps the starkest example of the intractable nature of the current regulatory scheme. The regulations were first proposed by FDA in June 1983 as a means of making investigational drugs (especially those which had completed Phase 2 tests) available to patients with untreatable serious ailments. The agency took no action on the proposal until March 1987, when it again proposed the rule, citing advanced cases of AIDS as an example of where the proposal would apply. FDA admitted at that time that it "could justify publishing [its proposal] as a final rule at this time." Curiously, however, FDA did not do so. Instead, saying that it was moving with "an abundance of caution," it asked for more public comment.[13]

Well-Orchestrated Hearings. In retrospect it appears that political, not medical, caution was behind this delay. The idea of easing the burden of proof for cases of untreatable life-threatening illnesses was attacked by Congress, major drug companies, and former FDA officials. These attacks reportedly were welcomed by the agency.[14] A well-orchestrated congressional hearing raised the specter of terminally ill patients being fleeced by unscrupulous drug companies — apparently this outweighed the reality of such individuals spending their last days ensnarled in red tape or left to the mercy of foreign or black market drug suppliers. Large pharmaceutical firms, which have more resources to deal with bureaucratic red tape, opposed the proposal, while the smaller companies with fewer resources favored it.[15] FDA Commissioner Frank Young delivered the *coup de grace*, claiming that the Office of Management and Budget had overridden his own opposition to the proposal and forced him to proceed with it.[16]

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11 Kenneth Kaitin, Barbara Richard, and Louis Lasagna, *Trends in Drug Development: The 1985-86 New Drug Approvals*, 27 J. Clin. Pharm. 545-546 (1987).

12 *Idem* at p. 548.

13 FDA, Reproposed Rule, 52 Fed. Reg. 8850 col. 2 (Mar. 19, 1987).

14 "Experimental Drugs, Power and the Limits of Deregulation," *The Washington Post*, July 15, 1987, p. A21.

15 See, for example, "Plan To Speed Approval of Test Drugs Pits Small Companies Against Big Ones," *The Wall Street Journal*, April 3, 1987, p. 33; "Drug Lag Defenders," *The Wall Street Journal*, May 15, 1987, p. 14.

16 See note 14.

The final rule, issued last May, sets forth an evidentiary standard for treatment INDs that may turn out to be little different than that required for NDAs.[17] As of March 1, only 11 treatment IND applications had been received, of which only three have been granted. While FDA's position is that this level of usage was expected,[18] at least one FDA official, who asked not to be named, acknowledges that FDA's use of the new provision has been disappointingly sparse. Leaders of many homosexual organizations have been more blunt, accurately calling the procedures "a fast track with no trains" and "a political smokescreen, offering only false hope and empty promises."[19]

FDA AND THE AIDS EPIDEMIC

The AIDS epidemic has revealed the structural weaknesses of the drug approval process. The uneasy balance between reducing the risks associated with new drugs and making new drugs available to desperately ill AIDS sufferers has led to several very disturbing cases of administrative shortcomings and questionable FDA decisions. Among them:

Ribavirin. In April 1987, FDA denied a treatment IND for ribavirin, a drug under study as possibly delaying the onset of AIDS symptoms after infection by the virus. Although the drug company performing the studies claimed that the results showed the drug to be safe, FDA disagreed, stressing that subjects in one trial who received ribavirin fared worse than those in the control group, a charge widely reported in the press. In congressional hearings a month later, FDA Commissioner Frank Young attacked the methodology of the manufacturer's tests and Representative Ron Wyden, the Oregon Democrat, accused the manufacturer of a failed attempt to "hot-wire" the regulatory system through a publicity campaign. In August, the manufacturer's treatment IND request was turned down for a second time. Yet only two months later, on October 16, the agency quietly reversed itself, stating that a review of the data "indicated that our safety concerns are not of sufficient magnitude to withhold approval of further clinical studies."[20]

VaxSyn HIV-1. Under FDA regulations, IND applications take effect 30 days after they are submitted unless FDA places a clinical hold on them. Yet the agency took nearly six months to approve the IND for VaxSyn HIV-1, the first AIDS vaccine to be tested on humans in the U.S.[21]

Peptide T. National Institute of Mental Health researcher Candace Pert sent samples of peptide T, a protein derivative that appeared to inhibit replication of the AIDS virus, to a doctor in Sweden's Karolinska Institute who had requested them. The Swedish doctor began small-scale human tests of the substance. The NIMH researcher, however, had not

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17 52 Fed. Reg. 19,466 (May 22, 1987).

18 Conversation with William Hubbard, FDA Director of Program Management, Office of Executive Operations, March 1988.

19 "False Hope: Smoke & Mirrors From the FDA," *PI Perspective*, October 1987, p. 1 (Project Inform, San Francisco, CA).

20 "FDA Allows Clinical Testing For AIDS Drug," *The New York Times*, October 20, 1987, p. B24.

21 F-D-C Reports, August 24, 1987, p. 7.

realized that sending an unapproved drug to another country for tests violated FDA regulations. Subsequently Pert had to suspend her shipments. [22]

AZT. *The New York Times* reported last December 28 that "the largest and most important clinical trial of an AIDS drug in the United States is lagging, with only half the needed patients enrolled." The substance being tested is AZT, a highly toxic drug and the only one approved for the treatment of advanced cases of AIDS. The trial, designed to determine AZT's effectiveness when administered early in the course of the disease, had its sponsoring agency changed, its methodology altered, and its supply of AZT restricted. The AZT test also suffered from a shortage of qualified medical personnel and even of volunteer subjects. Many AIDS victims did not want to take the risk of being placed in the control group, which would receive only a placebo treatment.[23]

In the view of some experts, the problem of drug unavailability ironically has been aggravated by the AZT approval process. A number of observers charge that the federal health establishment has become so preoccupied with AZT that trials of other promising drugs have suffered. According to David Barr, an attorney for the Lambda Legal Defense and Education Fund, "AZT is a highly toxic drug that cannot be tolerated by almost half of those seriously ill with AIDS. Yet, more than half of the Government-sponsored clinical trials involve AZT. Other drugs that appear to have lower levels of toxicity are not being pursued with the interest and intensity accorded AZT." [24]

Bureaucratic Interference. Whether or not these charges are true, the emphasis on AZT by federal agencies typifies the tendency of a centralized regulatory and research system to focus on a select number of favored approaches to the exclusion of less popular alternatives. To this is added the power that flows from control over research funds. The result is extensive bureaucratic interference with the independent judgment of the medical profession. Notes AIDS activist Larry Kramer: "I have talked with doctors across the country. Most are reluctant to speak for the record – an act that often jeopardizes their grants from Government agencies such as the National Institutes of Health, or even further chokes their relationship with the FDA."[25]

This situation is not unique to AIDS. Robert K. Oldham, chairman of Biotherapeutics, Inc., a pioneer firm in conducting cancer research for private patients, states that "the current research-regulatory alliance in cancer consists of the National Cancer Institute, the pharmaceutical industry, some 20 federally supported cancer centers, and FDA....This alliance has established a process that tests only a few drugs on patients each year....Moreover, the best and most exciting drug treatments are restricted to a small number of patients....While there are few data to support the need for this restrictive approach, the strategy remains a dogma of the research-regulatory process."[26]

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22 "Debate Over Potential AIDS Drug," *Science*, July 10, 1987, pp. 128, 130.

23 "Trial of AIDS Drug in U.S. Lags," *The New York Times*, December 28, 1987, p. 1.

24 Letter to the Editor, *The New York Times*, January 21, 1988, p. A27.

25 Larry Kramer, "The FDA's Callous Response to AIDS," *The New York Times*, March 23, 1987, p. A19.

26 Robert K. Oldham, "Whose Life Is It Anyway?" *The Wall Street Journal*, April 24, 1987, p. 10.

GOING IT ALONE

Faced with a scarcity of officially authorized drugs, AIDS victims are turning to foreign drug sources, black markets, homemade therapies, and organized self-help. Examples:

♦ ♦ In his book *And the Band Played On: Politics and the AIDS Epidemic*,[27] Randy Shilts describes how a community of American medical exiles quickly formed in Paris after word spread of a new French treatment for AIDS. Some arrived in such a weak state that they needed ambulances to transport them from the airport. Shilts also reports how isoprinosine tablets, available in Mexico, increased ten-fold in price by the time they reached San Francisco.

♦ ♦ Project Inform, a San Francisco-based self-help group, distributes a pamphlet entitled "Federally Unapproved Medications for Treatment of AIDS and AIDS Related Conditions (How to Get Them; How to Bring Them Home; How to Use Them)." It contains detailed information on various drugs together with reprints of medical journal articles, and offers advice on dealing with U.S. Customs officials, directories of "guerilla" clinics and cooperative physicians, and a street map of downtown Tijuana, Mexico.

♦ ♦ The *New York Native*, a homosexual-oriented newspaper, on March 9, 1987, provided two recipes for homemade versions of AL 721, a nontoxic egg lipid derivative that has shown promising therapeutic results abroad but is still unavailable in this country. The paper also carried advertisements for commercially produced egg lipid products (none of them by the U.S. licensee for AL 721, who is awaiting FDA action on its application).[28]

♦ ♦ A news article on AZT reports that many doctors are administering the drug to patients who have been exposed to the virus but have not yet developed the level of symptoms for which FDA authorized AZT use. Other physicians are reported to be "deeply alarmed, saying they could not recall another case when a drug with such toxic potential had been so widely prescribed for a condition other than those specified" by FDA. Physicians, who advocate such use, are said to be just as alarmed by "what they regard as the slow pace of Government-sponsored research."[29]

The patients, doctors, and others involved in such activities are trying to save lives, yet for many of them, their conduct carries the uncomfortable taint of dubious legality. In some cases their actions clearly are against the law. The culprits, however, are the laws that make people who are fighting for their lives act and feel like criminals. Charges Larry Kramer: "there is no question on the part of anyone fighting AIDS that the FDA constitutes the single most incomprehensible bottleneck in American bureaucratic history — one that is actually prolonging this roll call of death."[30] While this view may be overly magnanimous toward other bureaucratic bottlenecks in U.S. history, Kramer's charge has merit.

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27 New York: St. Martin's Press, 1987.

28 *New York Native*, March 9, 1987, p. 28.

29 "Doctors Stretch Rules on AIDS Drug," *The New York Times*, December 21, 1987, p. 1.

30 Kramer, *op. cit.*

Offering Some Hope. This dilemma has prompted a number of organized responses, from information clearinghouses to community-based research projects, which seek to provide AIDS sufferers with some hope, and possibly effective treatments. Project Inform, for example, collects detailed self-reporting questionnaires from individuals utilizing various AIDS treatments. Without such an effort, information available from the experiences of thousands of AIDS victims would be lost, and sufferers would be unable to distinguish between treatments that appear valueless and those which may have at least some potential. In New York, the nonprofit Community Research Initiative has been created for the purpose of expanding the number of clinical trials of experimental drugs. One of its goals is to sponsor tests of inexpensive, generic substances whose potential as AIDS therapies holds little financial promise for drug companies.

State governments also are beginning to react to the FDA bottleneck. Last September, California enacted a law under which it will test and possibly license AIDS therapies for sale within its borders, and several other states are considering similar measures.

WHY FDA ERRS ON THE SIDE OF CAUTION

Why is FDA such a bottleneck? The simple fact is that FDA has far more to lose when it mistakenly releases an unsafe drug than when it mistakenly delays an effective drug, even though both errors can cost lives. For this reason, the agency invariably will be overcautious in evaluating new drugs. Noted the University of Chicago's Sam Peltzman in a 1974 analysis of drug regulation: "Surely, no FDA official who has assisted the speedy introduction of a highly beneficial drug has received anything remotely resembling the public accolades accorded the colleague who prevented the marketing of thalidomide."[31]

Even more compelling is fear of criticism. Says former FDA commissioner Alexander Schmidt:

> ...in all of FDA's history, I am unable to find a single instance where a Congressional committee investigated the failure of FDA to approve a new drug. But, the times when hearings have been held to criticize our approval of new drugs have been so frequent that we aren't able to count them. The message to FDA staff could not be clearer. Whenever a controversy over a new drug is resolved by its approval, the Agency and the individuals involved likely will be investigated. Whenever such a drug is disapproved, no inquiry will be made. The Congressional pressure for our negative action on new drug applications is, therefore, intense. And it seems to be increasing ....[32]

31 Peltzman, *op. cit.*, p. 83.

32 Alexander Schmidt, quoted in Grabowski and Vernon, *op. cit.*, p. 5.

In large part this is due to the fact that the victims of a mistakenly approved drug are often highly visible, while the victims of a wrongfully delayed drug rarely even realize that they have been injured.

Ignoring the Lives Lost by Delay. The most recent example of this involves TPA, a genetically engineered drug capable of dissolving the coronary blood clots that cause most heart attacks. When administered within several hours of such an attack, it can restore circulation and minimize heart muscle damage. A 1985 federal study comparing TPA to another clot-dissolving agent found TPA to be so superior that the study was halted because physicians could not ethically continue to administer the inferior agent. Despite such data, an FDA advisory committee last May recommended against FDA approval of TPA. A half-year later, on the basis of supposedly new data (which confirmed the manufacturer's original claims), FDA Commissioner Young finally approved the drug.

Throughout this TPA episode, FDA apparently gave no consideration to how many lives were placed at risk by its delay. The transcript of the advisory committee meeting reveals much concern about TPA's safety, but absolutely none for the number of deaths that might occur during the time needed to gather additional safety data. Commissioner Young eventually hailed TPA as a wonder drug. But when asked about the human cost of FDA's own inaction, he charged that such questions were motivated solely by stock market interests. The delay in approving TPA might have contributed to the needless death of approximately 3,000 Americans.[33]

REFORMING THE APPROVAL PROCESS

The AIDS crisis is unprecedented in the extent to which its sufferers recognize that they are also victims of FDA procedures. The FDA approval process, in fact, may not survive this new understanding of the bureaucratic roadblocks to making new drugs available. While some federal government role in approving new drugs may be necessary, just as necessary is a thorough overhaul of the approval process. "Fine-tuning" the process is not enough. The underlying problems must be addressed. The institutional incentives that bias the process in favor of delay are simply too strong to be counterbalanced by some congressional or administrative directive to "speed things up."

FDA's role should be changed from a gate-keeper to an information provider. Rather than have veto power over new drugs, FDA should be limited to certifying them — judging whether they met the agency's criteria of safety and efficacy. Uncertified drugs could be marketed, but only under a system that assured both an acceptable degree of professional control over their availability and a full disclosure of risk to patients.

Prominent Warning. Under such a system, an uncertified drug would be available only by prescription. It would carry a prominent warning indicating that its manufacturer had not yet presented sufficient data on its safety and efficacy for the federal government to certify the drug. If appropriate, the warning could provide information on the availability of

33 Sam Kazman, "TPA Foot-Dragging Costs 30 Lives a Day," *The Washington Post — Health*, November 3, 1987, p. 6.

alternative, certified medications. The prescription would be accompanied by an informed consent document explaining the drug's uncertified status.

While uncertified drugs would become available, there still would be important and necessary restraints on their use. In particular, physicians would have to have some strong professional basis for prescribing an uncertified drug, especially if certified alternatives were available. The reason: medical malpractice laws would force physicians to balance the potential risks and benefits to the patient, and to make the risks very clear.[34] Moreover, malpractice insurers would take steps in their policies to ensure that physicians exercised great care and judgment in prescribing uncertified drugs to minimize potential liability. Prescribing an uncertified drug thus could become equivalent to a physician recommending a pioneering form of surgery, involving a high degree of risk, for a patient with a very serious condition who has not responded to other, well-tested treatments.

Allowing for Diversity in Circumstances. Such a reform would end the FDA bottleneck problem. At the same time it would preserve the agency's evaluative functions, to which the public attaches substantial importance and upon which Americans could continue to rely if they so chose. FDA might continue to act overcautiously, but the potential harm to seriously ill Americans from its doing so would be minimized, since the agency no longer would have a monopoly in judging new drugs.

Dale Gieringer, an analyst affiliated with Stanford University's Decisions and Ethics Center, favors transforming FDA into a drug certification – rather than approval – agency. He explains: "drug safety can be meaningfully defined only in terms of individual choice, not society-wide judgments of 'safety and efficacy'."[35] Only such an approach allows for the diversity in values, circumstances, and acceptance of risk that is inherent among human beings. Clearly an American suffering from AIDS, faced with almost certain death, should not be denied hope by an FDA official who is concerned about either possible side effects or about attacks from the press.

The Importance of Liability Reform

FDA's approval power, of course, is not the only obstacle to the availability of drugs. While permitting use of non-FDA approved drugs would eliminate the barriers caused by bureaucratic FDA procedures, the U.S. tort system can also be a formidable and unreasonable barrier to therapeutic access. Even in the area of experimental drugs, where patients are willing to assume some risk, liability insurance problems of physicians and drug companies sometimes severely restrict the availability of desperately needed therapies.

This is because under current law in many states, patients are prevented from voluntarily assuming a risk from a drug, even when they face certain danger if they do not take the drug – and even if they are desperate to take that risk.

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34 Of course, as noted below, the current malpractice system is far from perfect, and itself requires reform. Yet these problems cause the system to overcompensate for the risk of a few drugs rather than to undercompensate. Thus, even if the liability system were not reformed, the result would be too few new drugs prescribed, rather than too many.

35 Dale Gieringer, *Compassion Vs. Control: FDA Investigational-Drug Regulation*, *Cato Policy Analysis* No. 72 (1986), p. 24.

This liability problem is largely an issue of state, rather than federal, law. The states are beginning to take steps, such as reforming "joint and several liability" laws, but they also need to reform liability laws to increase the ability of individuals to allocate risk.

At the federal level, some reforms also are needed. Example: under FDA's rules for informed consent, participants in drug trials are forbidden to waive any legal rights.[36] FDA should explore ways to allow patients to make such waivers. This not only would increase their access to needed drugs, it would facilitate development of such drugs for others.[37]

CONCLUSION

The current drug approval system, allowing the FDA to bar new drugs from the market, must be reformed to allow patients to use non-approved drugs with a doctor's prescription. The FDA would continue to certify new drugs, providing the medical community with important information on drug safety. The resulting system would be much like that used for non-drug medical procedures, where doctors and patients may decide, without federal approval, whether a particular procedure is worth the risk.

A second obstacle to the availability of needed new drugs is the liability system. The states and the federal government should explore ways to increase the ability of individuals to voluntarily assume the risks of new treatments so that desperately needed drugs do not remain unavailable because of liability insurance problems.

Underground networks, illicit border crossings and guerrilla activities are terms normally associated with rebellions against totalitarian regimes, not responses to public health agencies. Just as a government may be judged on the basis of how its citizens vote with their feet, so FDA can be judged by how AIDS victims vote with their bodies.

Given the returns thus far, the mandate for change is clear.

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36 21 C.F.R. sect. 50.20

37 The use of private contracting in medical care as a means of addressing tort issues is receiving renewed attention. For an overview of research in this area, see American Hospital Association, *Nontraditional Approaches to the Medical Malpractice Crisis* (Legal Memorandum No. 12, December 1987).