done as a cure-all for a serious social, psychological, and political problem," said Newman. "But at the same time you can't turn down what is a highly successful form of treatment for some people."

Such arguments have persuaded most officials here that methadone is worth a huge expenditure, and barring a major new breakthrough, this drug is likely to remain the main form of treatment for American heroin addicts.

If legal methadone treatment is offered so readily why then is there a black market and where does the street methadone come from? For one thing, expansion of the facilities has not yet matched the demand. Waiting time for an addict to be enrolled in a publicly supported clinic in New York is now between 2 and 6 weeks (compared to 6 months a year ago). Moreover, many addicts simply have no use for the inevitable red tape and inconvenience involved in attending a clinic—they would rather pay $5 per day and take care of themselves. Others are hoping that reasonably pure heroin will again be available soon, and they're just marking time.

One source of street methadone is the addicts themselves who enroll in a program and then sell all or part of their daily dose. A number of profit-making methadone clinics are known to require only minimal identification, and thus an addict may be able to enroll in more than one and sell his excess supply. (Regulations recently published by the U.S. Food and Drug Administration for the use of methadone are designed to cut down this type of diversion.) The massive quantities available on the black market have led many people to speculate that there must be some diversion from the manufacturer or through the distribution system. Spokesmen for Eli Lilly and Co. insist that the drug is sold only to federally licensed clinics. Addicts maintaining themselves on illegal methadone generally take one-half to one-third the dose given in programs.

The fact that methadone has reduced drug-related crime and has not led to the addiction of many persons with no history of heroin abuse is not lost on law enforcement officers. They seem to be ignoring the methadone black market. In New York, sale of methadone is a crime with a maximum penalty of 15 years in prison. Yet methadone sales are carried out with few of the precautions that usually accompany heroin transactions, and police records show few arrests for methadone sales.

At the federal level, there also seems to be a policy of "benign neglect" of the methadone diversion. Myles J. Ambrose, President Nixon's special adviser on drug law enforcement and Deputy Assistant U.S. Attorney General, was asked in a recent interview if the government was not cracking down much harder on heroin than on methadone.

He replied: "I wouldn't want to be quoted as saying anything like that. We're certainly not in favor of illegal methadone. But we have to keep a balanced approach. We want to be sure there is treatment available for all addicts before we come down hard on the illegal methadone.—ROBERT J. BAZELL

Bazell, formerly a reporter for Science, *now writes for the New York* Post, *reporting on drugs and other health topics.*

Drug Regulation: FDA Replies to Charges by Economists and Industry

Milton Friedman, the Chicago economist whose conservative philosophy dominated much of President Nixon's first term, stepped out last month to deliver a swingeing attack on the Food and Drug Administration (FDA). In terms of human suffering, he stated in an article in *Newsweek*, the public forfeit caused by the agency's delay in approving beneficial new drugs more than offsets the gain of being protected from dangerous drugs. The legal basis on which the FDA requires drugs to be proved both safe and effective, the Kefauver amendments of 1962, should be abolished, Friedman said, and maybe the FDA along with them.

The risk-benefit question raised by Friedman touches a crucial factor in the regulation of drugs. The FDA often ignores its many critics, but this was one it could not let pass. Hearings held this month before Senator Gaylord Nelson's (D–Wis.) monopoly subcommittee provided an arena in which the FDA came out fighting from its corner. In a 133-page statement, the director of the FDA's Bureau of Drugs, Henry E. Simmons, produced a detailed and sometimes eloquent defense of the FDA's performance.

Friedman's critique cited a "brilliant paper" by Sam Peltzman, an economist at UCLA, on the effects of the 1962 amendments. Peltzman assigned dollar values to the benefit from suppressing harmful drugs and to the harm from delaying the introduction of successful ones. He estimated the cost of a delay at 10 to 100 times the value of avoiding a thalidomide type mistake. For instance, to have postponed by 2 years introduction of the drugs that cure tuberculosis would have caused about 45,000 additional deaths and 90,000 extra cases of the disease. According to the Peltzman thesis, the 1962 laws requiring drugs to be safe and effective have cost consumers of drugs, over and above any benefits, $250 to $500 million per year at the very least, equivalent to a 5 to 10 percent tax on drug sales. The 1962 laws, Friedman concluded, "should be repealed. They are doing vastly more harm than good. To comply with them, FDA officials must condemn innocent people to death."

The FDA does not see its role this way. If anyone has massacred the innocent, it is the drug companies, Simmons' testimony suggested. After the 1962 laws were passed, the FDA had the National Academy of Sciences review the effectiveness of the 4300 drugs put on the market in the previous 24 years. For only two drugs out of every five could substantial evidence of effectiveness be found. Of 16,000 therapeutic claims made by manufacturers, there was evidence to support only one in five. To waive the requirement for proven effectiveness, as some critics want, would be to return to the errors of the past. And the eliminations of ineffective drugs is perhaps as important

an advance in medical therapy as the discovery of new drugs, Simmons said.

In response to the criticism that the FDA worries too much about the safety of drugs, Simmons offered these considerations:

► The overprescription of drugs by doctors has created a major health hazard. Every year up to one and a half million people—between 3 and 5 percent of all hospital admissions—are admitted primarily because of drug reactions. Once in hospital, between 18 and 30 percent of all patients have a drug reaction. The length of their stay is about doubled as a result, with staggering economic consequences.

► The greater the public's use of drugs, the safer drugs need to be. Present exposure already amounts to more than 2 billion prescriptions and tens of billions of doses per year.

► The marketing of unsafe drugs offers an open-ended opportunity for tragedy. Thalidomide, marketed abroad but not in the United States, was associated with birth defects in more than 10,000 children. A less well-known case is a surge of asthma deaths that "may well be one of the greatest recorded therapeutic disasters in modern medical history." Use of an aerosol nebulizer containing a high concentration of isoproterenol seems to have caused some 3500 excess deaths of young children in England and Wales over a 7-year period. The drug was not submitted for approval here, but careful testing in humans and animals would have been required if it had been.

► An epidemic of pulmonary hypertension, a rare and often fatal condition, occurred in Switzerland, Austria, and Germany in the late 1950's. The condition seems to be associated with an appetite-suppressing drug, Aminorex. The FDA has been considering the drug since 1962 but has never allowed widespread human trials because of doubts about its safety. Even limited testing in humans was halted in 1968, "thus preventing a needless tragedy in this country which might have occurred with widespread, long-term use."

► Other examples of drugs which are marketed in other countries but which the FDA considers unsafe are a hypotensive agent from which more than a quarter of the patients developed abnormal liver function; a tranquilizer associated with suppression of blood formation in dogs, cleft palate in rodents, and disturbance of liver function in humans; and a number of beta-blockers in which there is an as yet unresolved problem with carcinogenic effects in animals.

The FDA is often blamed for the declining number of new drugs introduced into the country each year. But the decline in new drugs is a worldwide phenomenon that started 6 years before the effectiveness requirements came into being, Simmons contended. Most of these are recombinations or reformulations of existing new drugs. The number of genuinely new drugs marketed in the United States has remained stable for the past 22 years, numbering about 5 to 7 per year. As to the criticism by Friedman and others, that American citizens are deprived of useful drugs by the FDA's dilatory procedures, Simmons produced comparative figures showing that, out of hundreds of drugs introduced between 1966 and 1970 into France, England, or Germany (but not the United States), only four were marketed in all three nations. Of the four, rifampicin was admitted by the United States in 1971; flufenamic acid, found to be toxic in animals, was withdrawn from trials by the sponsor; alcuronium chloride has not been submitted for approval by the sponsor; and glyburide is still under study, but four alternative drugs are already available.

There may be short-term delays in the admission of new drugs because the United States has stricter standards than all other countries except Canada and Sweden. Simmons submitted a list of 26 drugs currently marketed overseas but disapproved here because of problems the FDA had discovered with their safety or effectiveness.

A final criticism is that the FDA's regulatory system raises the cost of pharmaceutical research, causing it to shift to more favorable climates abroad, thereby jeopardizing the future of drug development in the United States.

It is true that the cost of research has gone up, but that has not driven drug companies out of business. According to Simmons, the American pharmaceutical industry now invests $680 million a year on research and development, 50 percent more than was spent 5 years ago. To exploit the lower costs and the expertise of scientists in other countries, American drug firms have been stepping up their investment

AMA Said to Kill Panel to Save Ads

The American Medical Association (AMA) has been accused of dissolving its Council on Drugs as a sop to the pharmaceutical industry, to whose advertising the association is allegedly beholden. In interestingly frank testimony before the Senate monopoly subcommittee, John Adriani, professor of surgery at Tulane University Medical School and a past chairman of the AMA Council on Drugs, asserted that the drug evaluation compendium prepared by the council was displeasing to the industry and that the AMA killed the council so as not to lose the industry's advertising in its own journals:

"The fact that the Council was dissolved as an 'economy measure' is laughable to one who knows the facts. For a number of years the AMA, which derives a large portion of its income for its annual budget from advertising of drugs, has been a captive of and beholden to the pharmaceutical industry. The pharmaceutical industry was far from pleased with AMA-DE [AMA-drug evaluations]. . . . The Council on Drugs was a body of independent thinkers who refused to follow 'the party [AMA] line.'

"The dilemma of the Board of Trustees is understandable. . . . They had no choice but to appease the pharmaceutical industry. There were only two possible solutions: (i) to either 'muzzle' the Council to the point of abolishment if necessary, or (ii) to forego income from advertising for its operating budget. As a result, the second edition of this well-received volume, which has reached the final stages of supervision under the close surveillance of the Council on Drugs, will be completed by the staff of the Department of Drugs. The staff is composed of paid employees of the American Medical Association. . . . Physicians will now again be compelled to rely upon the *Physicians Desk Reference*, a product supported by the pharmaceutical industry, for drug information. Thus the AMA has abrogated its responsibility of providing factual information on drugs to the physician in the public's behalf."—N.W.

abroad, although this amounts to only 9 percent of their total R & D expenditures. The pharmaceutical industry, Simmons averred, "remains one of the healthiest and most profitable industries of the nation."

Other witnesses at the Senate hearing generally supported the FDA, the consensus being that the agency's execution of the 1962 amendments had done far more good than harm. Even Joseph Stetler, president of the Pharmaceutical Manufacturers Association (PMA), said he was not calling for repeal of the 1962 laws. Stetler did point out that, of 70 new drugs discovered by American companies between 1967 and 1971, 47 were first marketed abroad, to be accepted in this country only after delays of months or years and that "even if everything we do here is necessary and correct, it is agonizingly and unnecessarily slow."

Another witness, Daniel L. Azarnoff, professor of medicine at the University of Kansas Medical Center, said that the United States approves new drug applications significantly later than does England, and the American public is obviously deprived of these agents for varying periods of time. But the physical harm done to the public, Azarnoff said, is "probably minimal, although the monetary cost I suspect is significant."

In a recent spat in the letters columns of *Newsweek*, Friedman accused FDA Commissioner Edwards of answering his article with a "bureaucratic conditioned reflex." The FDA is more used to being attacked, in public anyway, from the consumer rather than the industry side. Peltzman's "brilliant" analysis has not yet been published, which saved the FDA from having to answer on possibly embarrassing points of detail. But as for answering the general thesis at least, its reflexes seem to have been quite effective.—NICHOLAS WADE

Endangered Species: Diplomacy Tries Building an Ark

For the humpback whale, a host of spotted cats, and a passel of rare orchids—among dozens of other endangered animals and plants—an international diplomatic conference at the State Department in Washington this month may provide the last, best hope for survival as a species.

Formally, the meeting is described as the Plenipotentiary Conference to Conclude an International Convention on Trade in Certain Species of Wildlife. Less formally, it is a semipublic conference to complete some of the unfinished business left over from the United Nations' environmental meeting at Stockholm last June; it began on 12 February, and from then until 2 March, the delegates from some 100 nations will spend several hours a day thrashing out the final and, in many respects, most crucial details of an agreement to protect endangered species that has been evolving at the glacial pace of international diplomacy since 1963.

If it all goes as U.S. officials hope and expect, the 100 nations, including East Germany and the Soviet Union, will formally initial on 2 March an agreement to establish the most sweeping global mechanism yet devised for regulating international commerce in specimens and products of rare wildlife. The "working draft" convention presently on the table contains obvious limitations and some latent loopholes whose breadth will be determined by the conference delegates and their technical advisers over the next 2 weeks. The final product "probably won't satisfy everybody by a longshot," Russell Train, the chairman of the President's Council on Environmental Quality, told a recent news conference. "But it must be viewed as a tremendously important beginning."

Or, as an Interior Department official described his expectations, the convention "will not be solely responsible for salvaging anything. But we hope it will help save something."

In essence, the proposed convention would establish an internationally run system of export and import permits to regulate trade in plants and animals specifically listed in the agreement as being endangered. As it is now worded, the agreement proposes neither quotas for the "harvesting" of endangered wildlife nor direct prohibitions on the killing or collecting of protected animals and plants. In two alternative preambles, however, the agreement does express a need to recognize the esthetic, economic, nutritional, and scientific value of wildlife and the consequent need to preserve it.

To accomplish this, the agreement proposes two parallel sets of controls—one pertaining to a list of animals and plants that are declining in numbers but not threatened with extinction and a second, stricter set of controls pertaining to species whose survival is in question.

In either case, each individual nation (or an internal agency it designates as a "scientific authority") is left free to decide how many export and import permits it will issue for each listed species. The agreement does, however, endeavor to set limiting circumstances. Thus, delegates are presented with a choice of the following two major rules for nearly extinct species:

> No export permit shall be granted until the scientific authority of the State of export determines that such export shall not be detrimental to the survival of the species. . . .

Or, alternatively, no permit shall be issued until an exporting nation:

> . . . determines that such export will be for purposes which are not detrimental to the survival of the species, and which will further the restoration of the species or which are essential for human health research. . . .

The draft agreement goes on to say that the permit system is intended to impose a virtual ban on trade in nearly extinct wildlife and to exercise "strict control" on trade in those animals and plants deemed to be declining but not on the brink of extirpation. In addition, the U.S. delegation is pressing for adoption of a clause creating a special category of nearly extinct wildlife for which signatory nations would agree to issue no export permits at all. There is, however, some doubt as to whether this stricture will survie in the coming days of debate.