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February 8, 1973

Dr. Karl A. Hochschwender
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Dear Karl:

Following up in a general way on several of the matters discussed at our December 15 meeting, I thought it might be worthwhile if, firstly, we sent to you and all of the members of the Committee a series of three articles from the February 4, 5, and 6 editions of the Washington Post. As you will note, all three of the articles were written by Mr. Morton Mintz, a Post staff reporter who has become something of a consistent FDA watcher and analyst.

Mr. Mintz' writings will, of course, speak for themselves. On occasion he has been a vigorous critic of the Food and Drug Administration but at this time he appears to be more on the side of defending the agency and its efficacy.

The only reason I thought I would call this matter to the attention of our Committee is because I think it will serve to point up some of the comments I made at the December meeting about the fluctuating status of Washington opinion on the Food and Drug Administration, its present structure, and the possibility of future restructuring. The articles really do not deal with matters of direct interest to us since they focus on the drug situation primarily. What I think they do indicate is that the present way in which the Food and Drug Administration operates procedurally is being called into question by important spokesmen. This we consider to be quite healthy. It may even lead to significant changes at some point which could be of lasting benefit.

For those who might be interested in my personal opinion, I think I disagree with Mr. Mintz' apologia for FDA, but I also disagree with the much publicized Peltzman-Friedman concepts. As I see it, both points of view represent extremes. What is really needed is a more effective regulatory body and my view is that this would best be accomplished if the Food and Drug Administration were reconstituted along the lines of the independent agencies such as the Federal Communications Commission and the Securities and Exchange Commission, both reporting directly to Congress, but otherwise operating independently. Rather than burden you with any more of my own philosophical feelings, I will now leave this subject for you and the readers hereof to conjure with.

Relative to other matters which might also be considered in the nature of follow-up items on our last meeting, we would like to direct the Committee's attention to two reports which appear in the December, 1972 edition of Food and Cosmetics Toxicology (Volume 10, Number 6). A brief description of the articles, which should serve to let you know why we think the members of the Committee might be interested in seeing the same follows:

1. The first article begins on page 815 of the volume in question and is entitled "Migration of Additives from Plastics Films into Edible Oils and Fat Simulant." It was authored by K. Figge and relates to the report Dan Dixler and you gave more or less jointly relative to a synthetic triglyceride which may be used as a fat simulant. I suspect that most of our Committee members have access to Food and Cosmetics Toxicology so we are not reproducing the Figge article here. We would suggest that anyone who does not receive this publication consider ordering the December issue by writing to Pergamon Press, Ltd., Maxwell House, Fairview Park, Elmsford, New York 10523.

Perhaps it will be sufficient to give everyone a clue as to the significance of the article by Mr. Figge if we simply quote here the second paragraph of the Abstract of his paper:

> "The measurements showed organic solvents to be unsuitable as general fat simulants. The migration values of an additive from a plastics film into different edible oils were so similar that one edible oil could serve as a simulant for all others. However, the presence of other naturally-occurring substances makes the analytical determination of migrated additives in edible oils very difficult, so a synthetic triglyceride mixture with extraction properties similar to those of coconut oil was developed to serve as a standard fat simulant. Analytical studies with this fat simulant, HB 307, proved its advantages over coconut oil. Its suitability as a standard fat simulant was confirmed in migration tests."

2. The same edition of Food and Cosmetics Toxicology referenced above contains another report on BHT and BHA in the form of a lengthy article by J. R. Allen and J. F. Engblom of the University of Wisconsin, the article being entitled "Ultrastructural and Biochemical Changes in the Liver of Monkeys Given Butylated Hydroxytoluene and Butylated Hydroxyanisole." At least as we read this article, it adds still further weight to the conclusion that presently permitted levels of these two important antioxidants are quite safe and that, for example, the so-called FAO/WHO acceptable dietary intake

for the use of 0.5 milligrams per kilogram of body weight is a very conservative figure.

I hope that this general information which we are supplying will be of interest to many of you. I might also take this opportunity to mention that you should be receiving your copies of the December 15 Minutes very shortly, if you have not already done so. The reason I do mention this fact is because we have had a number of inquiries about the Minutes in the past several days and were surprised to hear that some had not received them in light of the fact that they were mailed by the SPI office at the end of January. I feel quite certain that the reason for the delay is because the mailing was made fourth class because the Minutes are quite bulky and it was, therefore, deemed prudent to send them by fourth class mail. In short, please be a little patient if you do not have your copy yet, but by all means let Charlie Condit know if you have not received the Minutes within the next week or two.

Cordially yours,

George A. Hoffman

Enclosures

cc: SPI Food, Drug and Cosmetic
Packaging Materials Committee

Should the FDA Be Dismantled?

By Morton Mintz

Regulatory agencies are criticized all the time for not enforcing the law the way one critic or another thinks it ought to be enforced. This has been the lot of the Food and Drug Administration ever since the first federal food and drug law was enacted in 1906. But for some time now, the FDA has been a target for those who would cripple it or abolish it altogether.

Most revisionist proposals enjoy brief publicity only to fade into obscurity. Such was the fate of bills sponsored by Sen. Mark O. Hatfield (R-Ore.) to transfer drug-regulatory functions from the FDA to the National Academy of Sciences. Such was the fate of a proposal by Richard M. Furland of Squibb Corp. to make the FDA "an independent regulatory agency reporting directly to the President."

Far more serious is a batch of pending lawsuits, some of which are before the Supreme Court. These lay down a collective challenge to the fundamental legal right and capability of the FDA to assure the safety and efficacy of medicines in the first place, rather than to the agency's performance in implementing the drug law.

Last February, a group of scientists led by Dr. Robert D. Dripps, vice president for medical affairs of the University of Pennsylvania, complained in a letter to Rep. Paul G. Rogers (D-Fla.) that the procedures used to evaluate and approve new drugs stifle "creativity," increase research costs, reduce the number of new drugs "and may be depriving the practicing physician of agents beneficial to patient care."

The complaint deeply troubled the FDA, partly for reasons that have nothing to do with its counter-charge that the complaint was factually inaccurate and invalid. One of the reasons for FDA concern is Rogers' position as chairman of the House Commerce Health Subcommittee which makes him a powerful figure on Capitol Hill. Another reason is that the complaint was persistently and massively publicized by Medical Tribune, which is distributed free of charge to physicians and which is supported almost entirely by pharmaceutical advertising.

The FDA saw its plight take a drastic turn for the worse within the last few weeks, when its very justification for existence came under devastating fire in newspapers and magazines intended for the public at large, including the financial pages of The New York Times; Barron's, and Newsweek.

Only after a 25-year fight was the first true federal pure food and drug law enacted, in 1906. The late Dr. Harvey W. Wiley, who led the battle, said that a "group of ghouls" had foisted on humanity "the most wretched and disgraceful evil": "quack medicines," mostly harmful, for which manufacturers claimed therapeutic omnipotence.

Wiley told of "headache powders" that addicted women, of "painkillers" that "usually depressed the heart of the victim" and "made the pain far worse," of cancer "cures." He told of mothers who innocently "doped their babies into insensibility at night with soothing syrups containing opium or morphine."

Wiley became the first head of what is now the Food and Drug Administration. In 1938, the FDA acquired major new powers as a result of 107 deaths caused by "Elixir of Sulfanilamide," in which the solvent was a chemical relative of a radiator antifreeze.

In 1962, the agency's powers were expanded anew in the wake of the birth of thousands of limbless Thalidomide babies abroad; only a few were born here.

But increasingly, frustrations with the FDA's performance have led some to urge possible repeal of the food and drug laws, reversing the philosophy adopted 67 years ago. This is the first of two articles analyzing such proposals.

Writers in each of these publications drew on a single source, a paper presented by economist Sam Peltzman of the University of California at Los Angeles at a conference on new drugs at the University of Chicago. Both Robert M. [illegible]berg, editor of Barron's, and Milton Friedman, the Newsweek columnist and University of Chicago economist, acclaimed the paper as "brilliant." Roger Klein, an Arthur Anderson Research Corp. economist writing in The Times, termed the paper "outstanding."

The basic question addressed by Peltzman was whether the public had benefitted by the 1962 amendments to the 1938 drug law. For the most part, these amendments required manufacturers to provide substantial pre-marketing evidence of efficacy, in addition to the pre-marketing evidence of safety required by the existing law. The amendments also tightened the requirements for safety and empowered the FDA to act against false and misleading promotion of drugs to physicians.

Peltzman concluded that the amendments have done far more harm than good and that the public would be well served by their repeal. Professor Friedman went further, if not all the way. To comply with the amendments, "FDA officials must condemn innocent people to death," he said in a full-page column in the Jan. 8 Newsweek. "Indeed, further studies may well justify the even more shocking conclusion that the FDA itself should be abolished."

With or without "further studies," no one in government today expects Congress to abolish the FDA, unless it does so in order to replace it with another regulatory device. At the same time, Friedman, who has been urging abolition of the FDA at least since 1968 without visible impact, this time set top FDA officials and even Capitol Hill critics of the agency shuddering.

The explanation, in part, is the difference in climate. Not long ago, for example, an aide to President Nixon, commenting on his views of regulatory agencies that oversee business, said, "He's not going to go out to find people who are bigger regulators, but people who want to deregulate."

More fundamental in the reaction of even FDA's critics to the new attack is the knowledge that regulated industries of any kind prefer the illusion of regulation to the absence of regulation: that is, a situation in which the public *thinks* it is being protected by the government when actually the Great Seal of the United States is merely being affixed to whatever industries want. "The part of wisdom is not to destroy the [Interstate Commerce] Commission, but to utilize it," a railroad attorney counseled as early as 1892.

As for the food and drug industries, (Friedman did not suggest that food regulation be saved should the FDA go under), the concern is that the professor's attitude will give the intries a big push toward illusory regulation.

It becomes important, then, to examine Peltzman's message. His paper is 125 pages long and was prepared for economists, but, fortunately, Friedman provided a layman's summary in Newsweek (the accuracy of which was attested by Peltzman in a telephone interview). Friedman said:

"The stiffer standards [set by the 1962 amendments] had a spectacular effect on the rate of innovation. In the 12 years prior to 1962, 41.5 'new chemical entities'—that is, really new drugs—were introduced on the average each year; in the next eight years, 16.1. And their introduction was delayed by two years on the average.

"Peltzman used highly imaginative techniques to assign dollar values to the benefit from suppressing harmful drugs or postponing the introduction of useful new drugs . . . To make sure that his results would hold up, he leaned over backward, overstating benefits from the stricter standards, and understating costs. And, of course, he recognized full well that dollar estimates are a pale reflection of the human benefit and harm in terms of lives saved and lost. But that seems the only feasible way to get a numerical measure that combines the value of comfort gained by relief of a minor distress, days gained by avoiding or shortening illness and lives gained by curing a hitherto deadly disease.

"He estimates that the 1962 drug amendments cost consumers of drugs—over and above any benefits—$250 to $500 million per year at a very minimum. This is 5 to 10 per cent of the money spent annually on drugs. It is as if a 5 to 10 per cent tax were levied in drug sales and the money so raised was spent on invisible monuments to the late Sen. Kefauver.

"To supplement this estimate, and to get some idea of the effects of regulation on the more dramatic mistakes and discoveries, Peltzman examined the costs to society of a thalidomide-type mistake, the benefits to society from a penicillin-type success (though the actual examples he uses include neither thalidomide nor penicillin), the frequency of such occurrences prior to 1962, and the areas, notably heart disease and cancer, where major discoveries are much needed for the future. He then makes the extreme assumption that *no* major innovation will be permanently kept from the market by the post-1962 procedures, that their only effect will be to delay an innovation by two years. Even with this extreme assumption, it turns out that the cost of delaying a beneficial innovation is something like 10 to 100 times the value of avoiding a thalidomide-type mistake. In human terms, the effects of the introduction of the drugs that conquered tuberculosis are dramatic. Peltzman estimates that postponing their introduction for two years would have meant about 45,000 additional deaths from tuberculosis, and twice that number of additional persons with tuberculosis, out of a much smaller population than today's."

Peltzman's analysis and Friedman's use of it grow out of a shared, fundamental economic assumption: The best of all regulators is the free marketplace in which the consumer, through the choices he makes, is sovereign.

Few question (at least openly) the application of the consumer-is-king doctrine to those areas of the economy in which he has the information a sovereign needs in order to reign.

But Congress decided long ago that consumer sovereignty and *caveat emptor* —let the buyer beware— are fatally deficient protectors of the public in those areas of health and safety in which consumers cannot possibly be adequately informed.

Advancing technology has only served to persuade Congress that it was right the first time around. *Caveat emptor*, for example, does not protect consumers from beef containing a cancer-causing growth stimulant in amounts so tiny that they can be detected only with radioactive tracers. Consumer sovereignty, whatever it may mean to economists, was of no use to blacks who for years were exposed to excessive radiation by X-ray technicians bizarrely instructed by textbooks and manuals that higher doses were necessary for "Negroid" persons.

The explanation for Congress's attitude is nowhere plainer than in the voluminous public record in the prescription-drug field. Here, as the late Sen. Estes Kefauver (D-Tenn.) said, he who orders (the physician) does not buy, and he who buys (the consumer) does not order. That is to say, Congress recognized that the layman, even when not incapacitated or unconscious, lacks the information he needs to prescribe for himself, and must be at the mercy of the physician. The doctor, consequently, becomes the "consumer" even if it is the patient who goes to the pharmacy. That is why the prescription drug industry spent $500 million to $1 billion last year (depending on whose estimate is used) to promote medicines to its market—200,000 practicing physicians.

Friedman mentioned the thalidomide episode more or less in passing, omitting mention of a few salient points.

This sedative in foreign countries caused the birth of an estimated 10,000 limbless babies. No counterpart for anything quite so awful has been shown to have resulted from the FDA preventing any drug from reaching the market.

In the United States, had thalidomide not been kept from going on sale, an estimated 10,000 American infants would have been born without arms or legs. The company that had been pressuring the FDA's Dr. Frances O. Kelsey to release thalidomide meanwhile was claiming that it had "firmly established the safety" of the drug with "both foreign and U.S. laboratory studies." The ultimate "buyer" that would have to "beware" was the fetus. How would it use *caveat emptor* to protect itself against a chemical passing through the placental barrier of a mother who got thalidomide from a physician who had been misled by the manufacturer, knowingly or not?

The deformaties caused by thalidomide could hardly have been more obvious. Moreover, the cause of the deformities was relatively easy to trace. Yet in several countries without regulatory mechanisms, sales of the drug continued uninterrupted for weeks and even months after a cause-effect relationship had been established and widely publicized.

Suppose that thalidomide had caused cancer rather than gross deformaties. Before this would have been detected possibly 20 years would have elapsed. By that time, probably no one would have been able to pinpoint the cause. Indeed, it was only through a stunning piece of recent medical detective work on a rare form of the disease that a link was demonstrated between the ingestion of a hormone called DES by women seeking to prevent miscarriage, and the occurrence of vaginal cancer in their daughters up to a quarter-century later. Again, it was the fetus that was the "consumer" and that supposedly was exercising "sovereignty."

MONDAY: Threatened Protections)

Analysis

The FDA: Battling and Embattled

(Second of two articles on the question of whether the Food and Drug Administration should be abolished.)

By Morton Mintz

Are we not "fed with the same food, hurt with the same weapons . . .?" asked Shakespeare's Merchant of Venice. "If you prick us, do we not bleed?"

Pharmaceutical companies, in most respects, are like other companies. They do business, prize investor confidence, try to increase profits. They also try to expand their markets, as do other ventures. This particular activity is extraordinarily restricted, because it is not possible to expand markets for medicines by creating genuine diseases. Yet drug houses have found ways to cope with this problem.

If, for example, a drug is inadequately tested, or is fraudulently tested (the Food and Drug Administration and congressional investigators have documented numerous cases of each), the product may be prescribed by doctors who have been erroneously led to believe that the product is safer and more effective than it truly is.

More frequently, market expansion takes the form of exaggerated, misleading and false or even simply unwise advertising and promotion of prescription drugs to the physician. Several times, the FDA has criminally prosecuted drug companies for false and misleading claims of safety and efficacy. On other occasions the agency has used another weapon, seizure of interstate shipments. Literally dozens of times, the FDA has forced manufacturers to admit in corrective letters to doctors or in corrective advertisements that they have overstated safety and efficacy and understated risks and disadvantages.

In one criminal case, a drug for premenstrual tension was claimed in ads in the journal of the American Medical Association to have no "contra-indications," that is, no medical conditions in which it should not be used. Actually, the manufacturer had acknowledged contra-indications in millions of official prescribing brochures.

One of the civil cases developed from a $1-million promotion falsely claiming that a drug approved for angina pectoris had been shown to improve the survival rate of hospital heart-attack patients.

A corrective letter was sent by a company that recommended a semi-synthetic penicillin for infections for which other safe and effective drugs were available; the danger here was that overuse of the semi-synthetic threatened to defuse a major reserve weapon against outbreaks of staphylococcus bacteria, which can cause severe and sometimes fatal infection.

Physicians, influenced by drug company promotion, even now are continuing the practice of so massively overprescribing and misprescribing antibiotics as to imperil the health and sometimes even the lives of millions, specialists testified on Capitol Hill last December.

All of this points to a fundamental question about a recent economic analysis by Sam Peltzman, an economist at the University of California at Los Angeles, which is being used as the basis for renewed suggestions that the FDA should either be abolished altogether or should be stripped of some of its major protective powers.

Peltzman's basic criterion for determining whether a drug was bad or good was simply the decisions doctors make in the marketplace. If over a long period of time they continue to prescribe a medicine, if it withstands the "ultimate test" of time, then by Peltzman's reckoning it is "good."

"I wouldn't feel disturbed if a doctor relies on that information which he thinks is most reliable," he told a reporter.

he did not, he said, use such criteria as was used in the 1960s by the FDA when a panel of 30 specialists, re[illegible]d by the National Academy of Sciences, found that physicians were irrationally prescribing antibiotic combinations, thereby needlessly inflicting hundreds of thousands of injuries a year and threatening worldwide disaster from the proliferation of treatment-resistant organisms.

Unlike economists such as Peltzman, scientists decades ago rejected the proposition that the impressions of physicians can be a tolerable substitute for adequate, well-controlled, bias-free studies done by experts.

"The average practicing physician—and I have trained hundreds of them—just does not have the time, the facilities, the skill nor the training to be an expert in the determination of drug efficacy," Dr. Louis S. Goodman, a leading pharmacologist and member of the Council on Drugs of the American Medical Associaton, has testified.

Among, say, 100 patients with pneumococci pneumonia, about 30 will die and the rest will recover without the use of any specific remedies. Suppose a physician prescribed aspirin, which has no effect on the recovery rate, and the patient recovered. This would "mean nothing with regard to the aspirin because seven times in 10 the patient would have recovered anyway," says a former chairman of the council, Dr. Harry F. Dowling.

In survey after survey, physicians in large proportions have been shown to be guided principally in their prescribing decisions by advertising and sales pitches of drug companies that began giving them gifts to win their favor while they were medical students.

This sort of influence has been diagnosed as probably the principal explanation for phenomena such as the needless deaths of thousands of persons, mainly children, who have been prescribed a powerful antibiotic, chloramphemicol, for conditions (such as colds) in which it is ineffective, or for diseases in which safer agents are available.

Questioned about why they have prescribed chloramphenicol, physicians have cited long experience in their private practices with the drug, on the basis of which they have pronounced it "safe."

But from experience with, say, a few hundred patients, how would such a physician know that chloramephenicol kills one user in 24,200 to one in 40,500, depending upon dose? How could he learn contemperaneously, if ever, if another drug were say, to cause cancer 20 years after it was administered?

The annual toll of adverse drug reactions requiring hospitalization has been put by the National Center for Health Services Research and Development at 1.5 million, of which 30,000 are estimated to be fatal; the added medical expenses amount to at least $1.1 billion Repeatedly, in unrebutted articles and testimony on Capitol Hill, drug specialists have pinned major responsibility for this toll on physicians who prescribe on the basis of industry advertising and promotion.

A further question about the competence of practicing doctors to as[illegible] medicines is the test of time m[illegible]tioned by Peltzman. The record, however, is replete with examples of worthless drugs that have passed that test. Archaic medicines such as strychnine continued to be prescribed "50 years after it has been established that they have no use in medicine," Dr. Walter Modell, a noted pharmacologist, pointed out in 1962.

During the 1930s large numbers of Southerners, denied a wholesome diet, fell victim to a serious disease called pellagra. Victims who went to bed and ate the very kind of diet that produced pellagra seemed, at a certain acute stage of the disease, to improve briefly. "Any treatment, any procedure used at such a time is followed by this nonspecific improvement," Dr. William B. Bean, a specialist in pellagra, has said. "Thus, everything that was ever used by physicians, and this included almost every drug available in the pharmacopoeia, was praised as a specific cure."

Citing the Peltzman analysis as an argument for the possible abolition of the FDA, University of Chicago economist Milton Friedman charged recently in a column in Newsweek that the Kefauver-Harris Amendments to the drug law, enacted in 1962, have hurt the public by delaying the advent of valuable new drugs. (The amendments tightened safety requirements and required manufacturers to provide more premarketing evidence of safety and efficacy.)

The implication is that new drugs are necessarily better than old ones (and, of course, better than none at all; Friedman does not discuss the possibility that other therapies such as acupuncture may have their uses but, offering no profit for a major industry, long go ignored).

But the record suggests that new drugs are sometimes worse. Often the FDA has allowed a new drug to go on sale, seen it exuberantly promoted to doctors, seen doctors exuberantly prescribe it—and then had to recall it because it was discovered to be doing more harm than good.

A memorable example was an anticholesterol drug called MER/29. The FDA finally had to take it off the market in 1962. Eventually MER/29 proved to have caused a classical triad of injuries—cataracts, loss or thinning of hair and severe skin reactions—in thousands of persons.

Other drugs continue to be massively prescribed today although some eminent scientists retain doubts about them.

The FDA allowed efficacious oral contraceptives to go on sale without requiring their safety to be demonstrated. Not until several years later was it established that the pills cause blood clotting diseases in some women. Might the pills have genetic effects on the offspring of former users? Might the estrogens in them cause cancer? The tests that would provide the answers have not been done.

In a letter countering the Friedman position, FDA Commissioner Charles C. Edwards said that the decline in the rate of introduction of new drugs, blamed by Friedman on the amendments, actually began some years before the ywere enacted. "Moreover, the decline has been worldwide, encompassing some nations that as yet do not have these requirements," Edwards said.

Recalling Friedman's use of an example of deaths attributed to a two-year delay in the introduction of a tuberculosis drug, Edwards said the example was "hypothetical. It never happened, and I am convinced it never will." He went on to say:

"... No Americans are being condemned to death or misery because important drugs are being held up. There are no miracle drugs available in other countries that are not available here. I am not aware of even one life-saving drug entity which is not available here because of our more stringent safety standards. Nor is research being stifled. Drug research is, in fact, healthy and growing. We have repeatedly challenged our critics to name one important drug development which is available outside the United States but not here. We have had no takers. We submit the same challenge to Newsweek's Mr. Friedman."

Friedman's reply to the challenge was published with Edwards' letter in Newsweek. After accusing the commissioner of a "bureaucratic conditioned reflex" barren of "a single fact in reply to my column," the economist offered examples of drugs available abroad but not here, "practolol and Oxyprenolol, to mention just two important in cardiology."

The FDA acknowledged to a reporter that the two drugs show promise for treating serious, irregular heartbeat; noted that no American pharmaceutical firm is doing the clinical testing needed if the drugs are to be given general approval; and pointed out that physicians can obtain the drugs on an experimental basis for treating patients who do not respond to a marketed remedy called Propranolol.

But there is a question that the FDA says it must face: "Are we able to rule out the hazard of possible cancer?"

The agency's Cardiovascular and Renal Advisory Committee, composed of medical experts in this speciality, "has recommended that the drugs be administered to patients when Propanolol or other treatment is not effective," the FDA told a reporter. But, it said, the committee also has recommended "further studies to evaluate the true nature of the cancer factor connected with these drugs."

Test Rules Defended By FDA

By Morton Mintz
Washington Post Staff Writer

The Food and Drug Administration, mounting a major counterattack on a new wave of critics who would weaken or even abolish it, testified yesterday that its strict rules for human trials and marketing of prescription drugs spared the United States from several calamities that occurred abroad.

A medicine for victims of bronchial asthma, never sold here, was linked to "an epidemic of deaths" in England and Wales during the 1960s, the FDA told a Senate hearing.

The agency said it blocked marketing of a weight-reducing drug even before recent studies associated it with an "epidemic" in Austria, Germany and Switzerland of a sometimes fatal lung disease that had been rare everywhere until the late 1960s.

Among about 25 other medicines that never made it to the American market were a drug to lower blood pressure that caused liver disorders in 84 per cent of those who ingested it, and a tranquilizer that caused similar disorders in 43 per cent of its users.

FDA Commissioner Charles C. Edwards and top aides assembled the evidence, much of it previously undisclosed, to rebut charges that Americans are being deprived of important new safe and effective drugs available elsewhere, and that the agency's implementation of drug-law amendments enacted in 1962 has decreased the number of important new drugs entering the market.

Sen. Gaylord Nelson (D-Wis.), chairman of the Monopoly subcommittee, opened a four-day hearing on the development and marketing of new drugs by declaring that those who made the charges have a "duty" either to document or withdraw them.

One of the critics, Dr. Robert D. Dripps, vice president for medical affairs of the University of Pennsylvania, has said he is too busy to testify, Nelson disclosed.

Another critic is economist Sam Peltzman of the University of California in Los Angeles, author of a widely acclaimed paper calling for repeal of the amendments.

Economist Milton Friedman of the University of Chicago used the Peltzman analysis to step up the attack on the FDA

to what Nelson termed "the point of irrationality." Nelson cited Friedman's column in the Jan. 8 Newsweek charging that the amendments force the FDA to "condemn innocent people to death." Friedman suggested the public might be better off were the FDA to be abolished.

The amendments require manufacturers to provide substantial evidence of effectiveness in the form of well-controlled clinical investigations, require informed consent from persons in drug experiments and tighten safety requirements.

The asthma medicine was responsible for what "may well be one of the greatest recorded therapeutic disasters in modern history," Dr. Henry E. Simmons, director of the FDA's Bureau of Drugs, testified.

The medicine, a concentrated, potent aerosol spray called isiproterenol, was marketed in the 1960s, under various trade names, by several companies in Britain and Europe.

In England and Wales alone, use of the drug was associated by Dr. Paul Stolley of Johns Hopkins with a "seven-fold increase in asthma mortality in only seven years," with 3,500 "excess" deaths, and with 7 per cent of all deaths in children 10 to 14 years of age, Simmons testified.

The FDA official said Stolley determined that the "epidemic" was averted in the United States because the drug was not licensed here. Actually, no manufacturer sought marketing approval. Had one done so, Simmons said, he would have been required to provide a pre-marketing demonstration of safety and efficacy with careful animal and human trials. The spray continues to be sold abroad.

The weight-reducing drug linked to an epidemic of lung disease is aminorex, sold as Menocil by the Swiss subsidiary of Johnson & Johnson's McNeil Laboratories.

Simmons testified that the FDA began monitoring the experimental use of aminorex in 1962 but never allowed it to go on sale. Switzerland approved it for sale in 1965. Three years later, the FDA required the McNeil firm to halt human testing, "thus preventing a needless tragedy in this country which might have occurred with widespread long-term use," Simmons said.

The drug to lower blood pressure, guanoxan, was on an FDA list of about 25 medicines currently sold abroad but barred from further human testing and marketing in the United States.

Guanoxan, sold abroad by the Pfizer Co. under the tradename Envocar, had side effects severe enough that 31 of the patients on it "had to discontinue therapy," Simmons said.

The tranquilizer associated with liver disorders in 43 per cent of its users was identified as clopenthixol, sold by the Ayerst Laboratories division of American Home Products Corp, as Sordinol. In newborn dogs the drug increased the fatality rate and in rodents it caused cleft palate, Simmons reported. Animal tests can signal risks for humans.

Geigy's Opopramol, sold in 54 counties, for the treatment of mild symptoms of mental disturbance, was tied to adverse effects on the reproductive systems of three animal species, Simmons said. In humans it was related to blood and liver disorders and a syndrome characterized by large blisters of the skin and mucous membranes and damage to internal organs.