VOL. 18, NO. 7 JULY 1963

Food-Drug-Cosmetic Law JOURNAL

A COMMERCE CLEARING HOUSE PUBLICATION
PUBLISHED IN ASSOCIATION WITH THE FOOD LAW INSTITUTE, INC.

The editorial policy of this JOURNAL is to record the progress of the law in the field of food, drugs and cosmetics, and to provide a constructive discussion of it, according to the highest professional standards. The FOOD DRUG COSMETIC LAW JOURNAL is the only forum for current discussion of such law and it renders an important public service, for it is an invaluable means (1) to create a better knowledge and understanding of food, drug and cosmetic law, (2) to promote its due operation and development and thus (3) to effectuate its great remedial purposes. In short: While this law receives normal legal, administrative and judicial consideration, there remains a basic need for its appropriate study as a fundamental law of the land; the JOURNAL is designed to satisfy that need. The editorial policy also is to allow frank discussion of food-drug-cosmetic issues. The views stated are those of the contributors and not necessarily those of the publishers. On this basis, contributions and comments are invited.

The FOOD DRUG COSMETIC LAW JOURNAL is published monthly by Commerce Clearing House, Inc. Subscription price: $20 per year. Single copies are $2 each. Editorial and business offices, 4025 W. Peterson Ave., Chicago 46, Ill. Printed in United States of America.

July, 1963
Volume 18 • Number 7

Second-class postage paid at Chicago, Illinois.

FOOD DRUG COSMETIC LAW JOURNAL

Table of Contents . . . . . July, 1963

VOLUME 18 NUMBER 7

Printed in the United States of America

REPORTS

TO THE READER

In reply to a gracious letter from Mrs. Harvey W. Wiley, 2345 Ashmead Pl., N. W., Washington 9, D. C., an old friend of The Food Law Institute and of the JOURNAL, Mr. Dierson extends for all of us affectionate regards, best wishes for continued years and relief from afflictions, and assurances that we propose to maintain her name on our lists as a very special subscriber. Readers may wish to add their own personal notes or encouragement. Mrs. Wiley writes:

"Dear Friends of The Food
Law Institute:

"This is a sad letter I am about to write. But old age compels me to do it. . I had the pleasure of knowing Charles Wesley Dunn and was present when The Food Law Institute was started a few years ago. I have enjoyed the copies of THE FOOD DRUG COSMETIC LAW JOURNAL, which I have been receiving. But Old Age is old age and there is no disputing the fact that the passing of time dims the memory and a person's energy.

"I am writing to say that I believe that it is best for you not to send me any more copies of THE FOOD DRUG COSMETIC LAW JOURNAL. It is too valuable to send to a person who is unable to read and enjoy all the interesting contents of these JOURNALS. I look forward to reading the article 'Record Inspections 1906-1963' by Mr. George McKray but probably will not be able to read the JOURNAL through from cover to cover of the June number.

"As the widow of Dr. Harvey W. Wiley, the 'Father of the Pure Food Law' I am very happy to have been a part of the history of the law drawn up after Dr. Wiley's death in 1930, from 1933 to 1938. During those years I was President of the American Pure Food League and took an active part in the drawing up of the amendments and planning which culminated in the law of 1938. Now, sadly enough I am stricken with arthritis and suffer a great deal and walk with canes. I am no longer active. All of what I have said leads me to the conclusion that it is best for you no longer to send me the JOURNAL. I am no longer able to enjoy it as I used to do.

"But I leave it to you to decide whether to continue to send me the JOURNAL or not. I only want to prevent loss to you if you consider that I am not getting enough out of the JOURNAL.

"With all good wishes and many many thanks for your great kindness, I am

"Sincerely yours,
"Anna Kelton Wiley
"(Mrs. Harvey W. Wiley)"

"Dear Mrs. Wiley:

"As Secretary of The Food Law Institute and Chairman, Editorial Board of the FOOD DRUG COSMETIC LAW JOURNAL, I acknowledge receipt of your gracious letter of July 19.

"In behalf of all here and of the readers of the JOURNAL I express our affectionate regards and deep sympathy for you in your afflictions. We have for so long drawn inspiration from your devotion to and support of sound food legislation and consumer protection that we voice the optimistic hope and prayer that you will overcome

troubles and enjoy continued years of happiness and fruitful work.

"As regards future copies of the JOURNAL—permit us to send them without interruption. We simply cannot bring ourselves to drop you, a cherished and charter subscriber, from a list which is honored by the presence of your name.

"I propose to publish your letter in a forthcoming issue of the JOURNAL in order to share it with your many friends. I do hope you will have no objection.

"Sincerely yours,
"F. T. Dierson"

About This Issue. — This month's JOURNAL contains a paper delivered at the Institute of Food Technology meeting by *Franklin D. Clark,* Assistant to the Deputy Commissioner of the FDA. The author takes a look at the field operations of the FDA with emphasis on inspectional techniques. This article appears on page 365.

In an interesting article which begins on page 372, *Ross B. Ellis* outlines the responsibilities and organization of the Federal Bureau of Narcotics. Mr. Ellis, a District Supervisor of the Bureau, declares that the primary concern of the Bureau is with the illicit traffic which caters to the abusive use of narcotics.

The conclusion of a two-part article discussing the issue contained in the new bill H. R. 6788, currently before Congress, is found at page 380. *George McKray* appraises the desirability of extending record inspection authority. He is a lecturer at the University of California at Berkeley specializing in the legal aspects of public health and medical administration.

The FDA's views on investigational drugs are explained by *Earl L. Meyers,* chief of the Controls Evaluation Branch of the Division of New Drugs, Bureau of Medicine. This informative explanation starts on page 391.

"The primary purpose of clincial investigations is scientifically reliable data. A clinical investigator walks where others fear to tread, works in a different area and must take full responsibility for his professional decisions as well as full recognition of his scientific obligations, including those to the patient, his profession, to society, to his personal philosophy, and to his code of ethics." This is the opinion of *Dr. George E. Schreiner,* whose paper, "Liability: Use of Investigational Drugs," appears at page 403.

The Commissioner of Food and Drugs, *George P. Larrick,* spoke at the recent Council on Consumer Information. He invited the Council to report anything detrimental to their interests that would come under the jurisdiction of the FDA, and said he hoped the Council would be "inquisitive and communicative." See page 414 for his report.

The paramount challenge of the 60's is to insure the safe use of a multitude of chemicals permitted in the production, processing and distribution of the nation's food supply: pesticides—food additives—color additives. This is the opinion of *K. L. Milstead,* Deputy Director of the FDA Bureau of Enforcement, expressed in an article appearing at page 421.

Vol. 18, No. 7 July, 1963

Food·Drug·Cosmetic Law
Journal

Inspecting Food Processing Plants

By FRANKLIN D. CLARK

This Paper Was Delivered at the Institute of Food Technology Meeting at Detroit, Michigan on May 28, 1963. The Author Is Assistant to the Deputy Commissioner of the Food and Drug Administration.

I AM INDEED PLEASED to have the opportunity to join the speakers on this panel and participate in this symposium on FDA and the food industry. My contribution will be a brief overlook of the field operations of the Food and Drug Administration with some emphasis on inspectional techniques.

First, let me describe a little of our organization. About 40 per cent of our staff of some 3,000 are located in Washington, and include executive, legal, administrative and scientific personnel. Sixty per cent are in 18 field installations located in principal cities throughout the United States, each responsible for a specific geographic area. Each of the field districts has an administrative, inspectional and laboratory staff.

Our field inspectors inspect food, drug and cosmetic processing plants and collect samples of products produced in these plants. Our field chemists, bacteriologists, and microanalysts analyze the samples. The field district director coordinates these operations and submits to Washington his recommendations for seizure, prosecution or injunction when such recommendations are adequately supported by the facts that have been developed. All of our staff, wherever they are located and whatever be their duties, are charged with the same primary purpose—to protect the health and welfare of the consumer and to protect the honest manufacturer from any unscrupulous competition.

Duties of FDA Inspectors

Plant inspection is the heart of our enforcement operation. The food and drug inspector is the "eyes and ears" of the Food and Drug Administration and is, therefore, the "front line" in maintaining the integrity of foods, drugs, devices and cosmetics. He inspects production, storage and distribution establishments; investigates injury complaints and outbreaks of poisoning; and reports evidence of violation of the various acts. He examines the sanitary conditions in manufacturing establishments, and techniques and controls employed in the processing, labeling and packaging of foods, drugs and cosmetics. Sanitation is, of course, a predominantly important factor in food industry inspections.

Section 402(a)(3) of the Food, Drug and Cosmetic Art defines a food to be adulterated if it consists in whole or in part of any filthy, putrid or decomposed substance or if it is otherwise unfit for food.

Section 402(a)(4) goes one step further and defines a food as adulterated if it has been prepared, packed or held under insanitary conditions whereby it *may* have become contaminated with filth or whereby it *may* have been rendered injurious to health.

An FDA inspector is motivated by these two sections of the law in his appraisal of plant sanitation. Likewise his training includes a reasonable amount of accurate information as to the habits of the animals and insects which commonly constitute the source of the filth found in food establishments. His task during a factory inspection is one of study of the conditions and storage of raw materials used and the sorting or preparation to which they are subjected before processing; the conditions to which the products are exposed during their journey through the establishment and the conditions under which finished products are stored.

What the Inspectors Look for

Through visits to several plants an inspector becomes trained by observation and example in the fundamentals of a variety of manufacturing operations and in the sanitary concepts of good manufacturing practices. He is aware of the significance of allowing a precooked product to set at room temperature all day before packaging for overnight blast freezing. He is alert to the placing of toxic insecticides or rodenticides such as 1080 and DDT in close proximity to foods. He notes the construction of bakery flour lines, confectionery sirup

lines, soft drink pipelines, or bins and storage hoppers in cereal plants from the standpoint of ease in disassembling for cleaning. The inspector must carefully note employees' habits such as nesting containers whereby adhering floor dirt is transferred from outside to inside, failure to utilize available sanitizing or washing facilities, or nervous habits of plant personnel picking, scratching or rubbing their clothing.

In addition to technical background training and previous experience, and other information concerning the industry and its products that may provide the inspector with a broad perspective, he prepares for an inspection with other data. Prior to going to the plant or factory he reviews any previous inspection report of that firm, gains an idea of its relative size, type of products and processing, and former conditions or practices.

Having armed himself with available information, he assembles the basic equipment that might be needed. Usually this will include a flashlight, portable balance, black light, camera, sieves, triers and other sampling equipment, including vials, jars, plastic bags, and other containers for sample collection. He will have proper attire for the inspection, including a white cap and clean coveralls or coat.

Now that he is prepared for the task and has arrived at the plant, the inspector proceeds in accordance with Section 704(a) of the Act. This section grants authority for an inspector to enter, at reasonable times, within reasonable limits, and in a reasonable manner, establishments which are involved in the manufacture, distribution or storage of foods, drugs or cosmetics in, or to be placed in, interstate commerce. The inspections are made without prior notification, but a written notice is required to be presented to a person in authority at the time of entry.

As part of an establishment inspection, the government representative will determine the names of persons responsible for the management of the concern as well as the present legal status. To aid in determining the relative seriousness of any noted violation, he will request information about the approximate volume of output of each type of product and the proportion of this output moving interstate. If an establishment is under other government inspection, such as that furnished by the Department of Agriculture, that fact will be noted and the inspector invited to participate.

The actual inspection of a food processing plant will likely follow the normal flow of manufacturing from raw material through to the

final finished, labeled product. The raw material storage area and the raw materials themselves are closely examined for signs of damage or contamination with any foreign material. The black light assists in detection of rodent defilement. Flour or other pulverized materials are sieved where there is any basis to suspect contamination with macroscopic sized objects such as insect larva. The quality of materials is studied for evidence of decomposition, spoilage, deterioration and other factors which might render them unfit for use.

The inspector is alert throughout the inspection for signs of insect or rodent activity. The insanitary significance of rodents in a food plant needs little comment. They have been notorious for centuries as carriers of disease and pestilence, either directly or as carriers of disease-bearing fleas. Their habit of dribbling urine as they run, excreting as they eat, and their prying, pilfering nature makes them a prime hazard to production of a clean wholesome product. Flies, cockroaches and other insects are, of course, per se objectionable in a food processing plant. Aside from the aesthetic considerations insects, particularly flies, are frequently implicated as disease vectors in food poisoning outbreaks. On the other hand, careless use of extremely poisonous insecticides and rodenticides may render foods injurious to health and in violation of Section 402(a)(4). Control procedures for rodents and insects must therefore be done only with adequate safeguards. The inspector will therefore inquire about such procedures and the products used.

Our field inspector pays careful attention to the conditions in which products are exposed during their journey through an establishment. He notes the physical cleanliness of the plant, sanitary facilities, location and condition of toilets, lavatories, presence of soap and towels, and numerous other factors that enter into actual sanitation or reflect the awareness of management for the principles of good sanitation. Bacterial pollution during manufacture of certain foods has special public health significance. In some establishments, such as crab meat packing or frozen precooked food plants, adequate refrigeration and extra sanitary precautions are necessary to prevent adulteration of the finished product. In these types of operation, it is essential to use equipment having a smooth surface resistent to water, oils or grease and an adequate cleaning and sanitizing program. The inspector checks for this. Surely hand washing and hand sanitization before handling food products of this type are basic to good manufacturing practices. In some plants, sanitization dips may

be available to personnel handling the foodstuff but not used. We have found others in which not even good handwashing practices were followed.

Delays During Manufacturing Process

Lags during the manufacturing process are matters of concern to the inspector. Clean scrap from cutting, molding or packing operations, as well as the occasional batch that does not turn out satisfactorily, is commonly found to be reprocessed. This may be a perfectly proper procedure but adds additional problems. Unless stored in a protective manner, accumulated material may deteriorate or be attacked by pests and upon reuse, may contaminate a large amount of clean product. The inspector's attention is attracted to products subject to drying, aging, tempering, or other holding involving exposure overnight or longer since they may be subject to contamination by nocturnal rodents and insects. Manufacturing delays are of major importance when encountered in connection with operations involved in the manufacture or preparation of some foods. Bacteria flourish in a moist, nutritious environment under warm temperature conditions and will increase in numbers in direct relation to the period of time during which they enjoy these favorable conditions. The inspector may therefore determine time and temperature of some processes and holding operations as a measure of sanitation and good manufacturing practice.

Word pictures are never as good as photographs or the actual objects themselves. In order to preserve or confirm his observations, the inspector may take pictures of plant equipment or of particular plant areas. He may collect samples of raw materials, in-process or finished products. Factory food samples, consisting of photographs, exhibits, samples of raw materials or finished products are a usual part of an inspection of a food processing plant. A receipt describing any such samples collected will be left with management at the end of the inspection, which will contain a brief description of the articles collected. If any food samples are examined in the laboratory for filth or decomposition, the results will be reported in writing to the firm. The samples themselves are sealed and handled so as to protect their integrity since they might be needed at some future time where their authenticity would be critical.

From our standpoint, convincing proof that a product has been prepared, packed or held under conditions whereby it may have

become contaminated with filth is the fact that it did become so contaminated. If the evidence presented to the supervisory officers indicates the possibility of contamination, "official samples" will be collected from shipments entering or in interstate commerce. The results of the examination of such samples are then considered by the district director along with the inspector's comprehensive report, in arriving at conclusions about the legality of the manufacturing plant and its products. The inspector will therefore obtain specific information concerning distribution of the finished product. In addition, because his observations may be important with respect to particular interstate shipments only if the date of packing and shipping and the date of inspection are reasonably close together, detailed information as to code markings, dates and time lag between manufacture and shipment are important.

While courtesy alone requires laying a proper background with the responsible management of the firm before the inspection is undertaken, courtesy and fairness and the law require a detailed discussion of the observations made with the management after the inspection. A written report will be furnished to a responsible official and will include all specific observations of (1) foods, drugs, devices or cosmetics deemed to be wholly or in part filthy, putrid or decomposed, (2) undesirable conditions or practices bearing on filth or decomposition, or (3) insanitary conditions or practices which might render a product injurious to health. The report will be a concise summary of observations to serve as a guide to plant personnel in taking corrective action. The significance of any observations set forth will be discussed orally if desired, but for obvious reasons the inspector will not assume the role of a pest control or equipment expert and dictate exactly what should be done. The methods employed for the elimination of the sources of adulteration are not the prime interest to the inspector so long as they are effective and are not of a character to cause some other nuisance.

What else does the inspector want by way of information when he inspects, in addition to observing general conditions and practices? He wants—no more no less—everything actually needed to reach a presumptive conclusion about the legality of the operation or the food produced. He wants to know, for example, what ingredients are being used. If the formula shows any food additives or color additives, he will want to know if reasonable controls and safeguards have been installed to see that all such materials are legally used and that there is no reasonable likelihood of accidental misuse. He wants to com-

pare the finished product label with the formula and the process to see if declared ingredients are actually included or if there are others which are not properly declared. He wants to know if the net contents are correctly declared on the label. Finished products in a factory, warehouse or other establishment are often weighed on a very accurate portable balance to determine the net weight. If specific gravity of a liquid is known, net volume can also be indirectly determined by use of net weight checks.

The law provides that unless there is a written agreement between shipper and consignee that the consignee will apply labels that fully comply with the law, unlabeled or partially labeled merchandise cannot be shipped in interstate commerce. If less than completely labeled goods are being shipped, the inspector will want to examine copies of any agreement and correspondence pertaining to such agreement.

Inspections are not guided by the desire for punitive action. There is a genuine desire that inspections be helpful and assist manufacturers in correcting any conditions observed which might lead to violations. Specific comment or warnings to responsible individuals will be confined to clear-cut violative conditions such as filth, decomposition or deleterious substances. While there are some elementary labeling matters the inspector will discuss, in the main he will recommend that labeling questions be taken up with the district office or with the FDA in Washington. The fact that he may collect labeling and offer no adverse comment at the time is not therefore to be construed as an "approval" or endorsement of such labeling.

In conclusion, I would like to repeat what the Commissioner recently stated before the Subcommittee on Health and Safety of the Interstate and Foreign Commerce Committee of the House of Representatives:

> A large part of our activity and the most important part in the final analysis consists of day-to-day operations all over the United States in which, without fanfare and without publicity, our scientists, whether in the laboratory or in the field, go about their job of safeguarding the food and drug supply of the Nation. . . . When one of our inspectors walks into a small manufacturing establishment to make an inspection, he represents, for the moment, the United States Government so far as that factory is concerned. The owner is not particularly concerned then about how the law got passed or who administers it in Washington. He is concerned with the visit of our inspector.
>
> We are proud of the way our men represent the federal government. They do a good job that is too often forgotten when the headline stories are written.

[The End]

A General Outline of Federal Narcotics Statutes

By ROSS B. ELLIS

The Author Is a District Supervisor of the Federal Bureau of Narcotics. He Presented This Paper Before the Tenth Annual Joint Pharmacy Seminar at Wayne State University in Detroit, Michigan, on February 26, 1963.

THE RESPONSIBILITIES of the Federal Bureau of Narcotics as fixed by Congress relate to opium, its alkaloids and derivatives, coca leaf and its derivatives, marihuana, and specifically defined synthetic substitutes known as "opiates." We do not have any responsibilities with regard to the so-called dangerous drugs, that is, barbiturates and amphetamines. Federal law prohibits the sale of amphetamines and barbiturates without a doctor's prescription, as you all are well aware. It also forbids the refilling of a prescription without the consent of the doctor. The Food and Drug Administration of the United States Department of Health, Education and Welfare is charged with the responsibility of enforcing federal law which relates to these drugs. It should be noted that the illegal sale and possession of these dangerous drugs is generally an offense under many state and local laws. Some confusion exists as to the nature and effects of these dangerous drugs. It is well to remember that these are legitimate and useful drugs, but only when used properly under the supervision of a physician.

These should not be confused with such drugs as heroin and marihuana, which are not in the pharmacopoedia of medicine. Whenever illegal use of barbiturates or amphetamines comes to your attention, the Food and Drug Administration should be notified. All of the substances with which the Bureau of Narcotics are concerned, except heroin and marihuana, also have a valuable place in medicine. While we do administer certain controls over licit manufacture and distribution of these drugs, our prime concern is with the illicit traffic, which caters to the abusive use of narcotics. I would like to take this opportunity to pay public tribute to all those, who in the course of their business or profession, manufacture, distribute or prescribe narcotic drugs. The bureau has had the very finest cooperation and help from these groups. They have most willingly accepted restrictions

and controls deemed necessary by the government to aid in the suppression of the illicit traffic and abusive use of these drugs.

Principal Drugs in Illicit Traffic

Opium and its derivatives—cocaine and marihuana—are the principal narcotic drugs in the illicit traffic today. Opium was first used as an anesthetic some 4,000 years ago, but the actual use for medical purposes was not understood until about the sixteenth century.

Morphine was not isolated until the nineteenth century and heroin is the twentieth century drug of addiction. Opium smoking was not begun until the art of smoking tobacco was acquired from our own American Indians. By the beginning of the twentieth century, mass addiction to the smoking of opium had prostrated China and opium smoking had spread to other countries, including the United States. Smoking of opium ceased to be a problem in the United States around 1910 when the importation of opium for other than medical purposes was prohibited. However, opium smoking continued to be legal in many countries in the world under government monopolies. It was not until after World War II through the action of former Commissioner of Narcotics Harry J. Anslinger, that smoking of opium was prohibited in all countries.

Cocaine was discovered about the middle of the nineteenth century, but coca leaf chewing had been practiced by the ancient Incas of Peru long prior. It is interesting to note that Peru remains one of the principal sources for licit stocks of cocaine today. The habit of coca leaf chewing is still prevalent in several South American countries today. It should be noted that cocaine is more a drug of the illicit traffic in the Far East than it is in the United States.

Marihuana was known 3,000 years ago in southern Asia and today is cultivated in many countries for cordage made from its fiber. It is interesting to note that a reference to marihuana and its alkaloids was contained in Homer's classic, *The Odyssey.* Also marihuana in the ancient Arabic world was known as "Hashshashin." The English word assassin has its origin in this Arabic term. It originally referred to one of a Mohammedan secret order, which, at the time of the Crusades, committed secret murders under the influence of hashish, which we know as marihuana. The resin contained in the plant is a prominent drug in the international traffic and is a problem in many countries.

The movement to control narcotics began in China and was followed swiftly by international conventions and agreements as well as by legislation in many countries. Heroin spread throughout the world in a little over 50 years, but it remains a legal drug in all but six countries today.

Bureau of Narcotics Established in 1930

Enactment of the Harrison Act of 1914 and the Import and Export Act of 1922 was followed by the creation of the Bureau of Narcotics in 1930. The Bureau today remains an enforcement branch of the United States Treasury and consists of 14 districts. Thirteen of these are in the United States with the remaining district in Europe with headquarters in Rome. It is noted that Detroit is the headquarters office for District No. 8, which encompasses the States of Michigan, Ohio and Kentucky. The bureau recognizes the international aspects of the narcotic traffic and continues to establish new offices throughout the world. The agents assigned to these offices cooperate with foreign representatives doing similar duties in preventing illegal shipments of narcotics from reaching the United States.

Legislation enacted by Congress has been of tremendous assistance in the control of illicit narcotic traffic.

Boggs-Daniel Narcotic Control Act

The narcotic problem in the United States in recent years has received wide public attention. During 1955 and 1956, two committees of Congress, a House Subcommittee headed by Congressman Hale Boggs and a Senate Subcommittee headed by Senator Price Daniel, made a nationwide survey of the illicit narcotic traffic. This comprehensive study of the narcotic problem in the United States by two separate committees of Congress resulted in the Boggs-Daniel Narcotic Control Act of 1956.

This new law provides more drastic penalties for the seller and smuggler of narcotics, with a minimum mandatory sentence of five years to 20 years for first offenses of sale of narcotic drugs of marihuana and 10 to 40 years for subsequent offenses, plus fines up to $20,000. It eliminated parole, probation and suspended sentences for these violators. It provides a specific penalty for the sale of heroin to a juvenile—10 years to life, and if the jury so recommends, the death penalty.

It also authorized the granting of immunity to a witness in a narcotic matter and provides for a broadened authority of the Bureau of Narcotics officials and agents and customs officers to make searches, seizures and arrests in the investigation and prosecution of narcotic violations, including the authority to serve a search warrant at any time of the day or night if there is probable cause to believe that grounds for its application exist.

The new law provided for the surrender of all stocks of heroin to the government and requires the registration of all addicts and convicted narcotic violators upon leaving or entering the United States.

Training School for State and Local Officers

The act also provided for the establishment of the Federal Bureau of Narcotics Training School for the training of local and state officers in narcotic law enforcement, so that these officers may cope with the narcotic problem on a state and city level. Every city with a narcotic problem of any consequence should have a special squad of men devoting full time to narcotic law enforcement. It is noted that here in Detroit, the Detroit Police currently has a Narcotic Bureau with a complement of 22 personnel. Since the establishment of the Federal Bureau of Narcotics Training School in October 1956, over 900 officers have received its specialized training, many of them from foreign countries. The Bureau of Narcotics, with its limited force of approximately 290 agents, has always acknowledged the important role, which local enforcement agencies play in narcotic law enforcement. Local and state narcotic enforcement officers have earned our gratitude for the splendid cooperation and assistance they have consistently given us in our fight against the illicit narcotic traffic.

Number of Addicts Has Decreased Since 1914

The Boggs-Daniel Control Act has provided us with an important weapon in the war against the vicious narcotic traffic. The federal legislation, in a relatively short time, has brought about a marked decrease in the illicit narcotic traffic in the United States. In many parts of the country, the traffic has been virtually eliminated. In the United States for example, in 1914, one out of every 400 people was addicted to the use of narcotics. In 1960, only one in every 4,000 was addicted.

Although the new narcotic law is aimed at the narcotic peddler and smuggler, we have found that there is some concern in the phar-

maceutical profession that a mere technical violation . the part of a pharmacist may subject him to the stringent penalties of the Boggs-Daniel Control Act. Let me put your minds at ease on this point immediately. We have yet to bring a pharmacist into court on a mere technical violation under either the new or the old law.

Technical violations of the law or the regulations through ignorance or carelessness are handled informally by the Bureau of Narcotics. We do not intend to change this policy and bring pharmacists into court for minor infractions of the law. The Bureau of Narcotics is primarily concerned with the illicit narcotic trafficker, the peddler and smuggler. If a pharmacist should fall into either of these categories, then of course we intend to prosecute him under the Narcotic Control Act of 1956.

The profession should know that pharmacists are receiving more consideration than heretofore from the Bureau of Narcotics. We intend looking into a situation only when we determine that a pharmacist is deliberately engaged in selling narcotic drugs for the purpose of gratifying drug addiction. Specific instructions have been sent to all our supervisors to refer direct to Washington all cases involving registered pharmacists. Before action is taken by the districts, the preliminary evidence is reviewed in Washington by a committee of bureau officials. This committee decides whether a full investigation looking toward prosecution should be instituted. No such procedure as this was followed prior to the Boggs-Daniel Narcotic Control Act.

Narcotic Problem Centered in a Few States

While the over-all picture of the narcotic problem in the United States is more encouraging than at any time in the past several years, we do still have a few isolated areas in the country that present a rather acute problem. One of the most serious situations is to be found in the New York area. In the State of New York alone are 46.6 per cent of the narcotic addicts reported for the entire United States. The State of Illinois has 14.8 per cent of the narcotic addicts reported; the State of California has 16.2 per cent; the State of Michigan has 4.2 per cent and the remaining 18.2 per cent are scattered throughout the other states. These figures which I just quoted reveal the results of a bureau survey ending December 31, 1961. As you see, the narcotic problem is concentrated in just a few states and even in these states is found mainly in the metropolitan areas of New York City, Chicago, Los Angeles and Detroit.

Ohio Legislation Proves Effective

Only a few years ago the State of Ohio was faced with a most serious narcotic problem. As a result of the efforts of C. William O'Neill, former Governor of Ohio, the Ohio legislature in 1955 put through a law which is one of the most stringent in the United States. It provides a minimum prison sentence of 20 years for the illegal sale of narcotics. The results have been startling, and demonstrate what effective legislation can do to control a serious narcotic problem. The illicit traffic in narcotic drugs in Ohio has dropped 85 per cent, and the number of narcotic addicts has decreased accordingly. Many of the peddlers convicted under this law have expressed the wish that they had left the narcotic traffic and gone into some other racket. Incidentally, many of the traffickers convicted under the Boggs-Daniel Narcotic Control Act have expressed similar views.

In spite of the few problem areas in the country, narcotic addiction is on the decrease. The greatest improvement is among the juvenile group. It is rather ironic that with this decrease in addiction, we still have a minority group attempting to convince the public that the only way to solve the narcotic problem is to make narcotic drugs freely available to the addict. They would have the AMA and the ABA sponsor the establishment of free dispensaries throughout the country furnishing the addict with all the narcotic drugs he can consume. As pharmacists, you know this would be disastrous, and I hope that you continue to resist any such program with all the facilities at your command.

International Narcotic Travel

Since smuggled heroin is currently our greatest problem in the illicit traffic, control of the international narcotic traffic is of the greatest importance. Heroin enters the United States from Europe, and the Near East, Red China and Mexico. Clandestine factories operating in France, Syria and Lebanon process opium and morphine base from Turkey, one of the major producers of opium. This heroin is eventually smuggled into the United States and Canada through France and Italy.

For the past several years we have had a complement of agents abroad assisting foreign police in intercepting shipments of heroin destined for the United States. They have been remarkably successful, and several important international gangs of narcotic traffickers have been eliminated.

While most countries are making some effort to control the illicit narcotic traffic, no such effort is being made on the part of the Chinese Communists. The illicit traffic in drugs from Red China flowing through Burma, Laos, Cambodia, Thailand, Hong Kong, Japan and into the United States continues to grow.

I should like to mention here that the United States has consistently led other countries in the worldwide struggle against narcotic addiction and the illicit narcotic traffic. We in this country are particularly fortunate to have former Commissioner Harry J. Anslinger as our representative on the United Nations Commission on Narcotic Drugs.

The United Nations Commission on Narcotic Drugs continues to urge all governments to increase efforts to detect and suppress illicit production and manufacture of narcotic drugs, to apprehend narcotic traffickers and to impose severe penalties on those convicted of narcotic offenses. As a result, just a short time ago the government of Iran placed a complete ban on the production and consumption of opium in that country. Previously Iran had been one of the major producers of opium, much of which found its way into the international traffic. Only recently the government of Afghanistan announced a similar prohibition on the production and consumption of opium.

Addicts Now Seeking Paregoric

In this country, in areas where the illicit traffic in heroin has been eliminated, a situation is developing which affects the pharmacist. We are now receiving reports from those areas that drug addicts are turning to paregoric. This has resulted in a virtual onslaught on the pharmacies of those areas by addicts trying to get enough paregoric to meet their needs.

Where a community is faced with this predicament, we believe that the responsibility for controlling the situation rests with the pharmacists. He is in a position to limit the sales of exempt preparations and prevent their use to maintain addiction. Some time ago, the pharmacists in Dayton, Ohio, faced with a "run" on paregoric, brought the problem under control quickly by agreeing to dispense paregoric only on a physician's prescription. As a result, the diversion of paregoric in Dayton has been eliminated.

The Bureau of Narcotics knows that the pharmacists will accept their responsibility, and we are confident that they can handle the

paregoric problem in their own communities. Therefore, when we notice a particular situation involving exempt narcotic preparations getting out of hand, we intend to bring it to the attention of the State Boards of Pharmacy and the state and county pharmaceutical associations, so that they can take necessary corrective action. We are not interested in imposing any additional restrictions on the pharmacist. The pharmacy profession should exercise its own controls in a situation of this kind.

In addition to the diversion of paregoric, we anticipate that there will be an increase in forged narcotic prescriptions and pharmacy thefts in certain acute areas. Here again the pharmacist can assist in controlling the situation; in the case of forged narcotic prescriptions, by knowing their customers and the prescribing physicians; in the case of pharmacy thefts, by properly safeguarding narcotic stocks.

The Oral Prescription Law, which has now been in effect for 5 years, appears to be operating satisfactorily, I am happy to say. On March 6, 1958, we had published in the *Federal Register* the first addition to the original list of narcotic drugs and compounds in the oral prescription category. This addition allows the pharmacist to follow the oral prescription procedure for any compound consisting of Dihydrocodeine or any salt thereof with one or more active non-narcotic ingredients in recognized therapeutic amounts where the content of Dihydrocodeine or any salt thereof does not exceed eight grains per fluid ounce or one grain per dosage unit.

I believe that many states have now amended their laws to conform with the federal procedure in permitting the acceptance of oral prescriptions for those narcotic drugs and compounds designated in the classification for which oral prescriptions are applicable. This procedure has relieved the pharmacist of some of the pressure of the former strict requirements for some of these drugs and has expedited service to the sick. We hope the pharmacists of the country will not abuse this relaxation from former strict requirements, since your own able representatives were responsible for bringing about this new procedure.

In the 32 years since the establishment of the Federal Bureau of Narcotics, we have consistently received the support of pharmacists in our mutual fight to keep the narcotic traffic under control.

The privilege to participate in this Seminar is another example of this support and cooperation. I am both honored and gratified by your attention. **[The End]**

Record Inspection 1906-1963

By GEORGE McKRAY

This Is the Second of Two Parts Discussing the Issue Contained in the New Bill H. R. 6788 Now Before Congress. The Author Is a Lecturer at the University of California in Berkeley Specializing in the Legal Aspects of Public Health and Medical Administration. During 1961-1962 Mr. McKray Was a Food Law Institute Fellow at the New York University School of Law.

THE DESIRABILITY OF EXTENDING RECORD INSPECTION AUTHORITY: COMMENTS ON GOVERNMENT AND INDUSTRY VIEWPOINT

AFTER THE PASSAGE of the Drug Amendments of 1962, the General Counsel for the United States Department of Health, Education and Welfare commented on the FDA's effort to obtain the right of compulsory record inspection as follows:

> There has long been a running dispute between the government and the pharmaceutical industry about the scope of the authorized inspection of manufacturing firms and their records. Such vital matters as formula cards, complaint files, and assay results have been withheld from us by many firms.
>
> Congress has made it plain in the new amendments that all information needed to determine whether the legal requirements are being met must be made available to authorized inspectors. With this authority, we will now be able to make more meaningful investigations of prescription drug manufacturers and control procedures and to check on the adequacy of record keeping and reporting. Without this authority, we were required to determine compliance solely by time consuming analyses rather than by utilizing the firm's own assay records for information about drug composition.[87]

Having obtained the record inspection power it sought with regard to the prescription drug industry, will the FDA renew its attempt to extend this authority to cover other industries? There is evidence that it will. On February 7, 1963, in a message to Congress relative to his Health Program, President Kennedy said:

> We cannot afford to withhold from the Food and Drug Administration the full authority required to provide the maximum protection to our families. I

[87] "Current Developments in Federal Law," an address by A. W. Willcox, Federal Services Pharmaceutical Seminar, Bethesda, Maryland, November 15, 1962.

recommend the enactment of new legislation to extend and clarify inspection authority to determine whether food, over-the-counter drugs, cosmetics, and therapeutic or diagnostic devices are being manufactured and marketed in accordance with the law;[88] . . .

Thus, it seems likely that the debate between government and industry as to the advisability of extending the FDA's record inspection authority will continue. In this section of the paper the two opposing viewpoints will be explored and appraised.

THE DEBATE ON NEED

An important issue is whether new legislation is needed to correct a situation in which industry is withholding from the government information necessary to safeguard the public.

Statements by the President and by the former Health, Education and Welfare Secretary made prior to the 1962 hearings, summarize the government's stand. They refer to the food, nonproprietary drugs, and cosmetics industries as well as the prescription drug industry.

On March 15, 1962, President Kennedy said:

> Factory inspections now authorized by the pure food and drug laws are seriously hampered by the fact that the law does not clearly require the manufacturer to allow inspection of certain records. An uncooperative small minority of manufacturers can engage in game of hide-and-seek with the Government in order to avoid adequate inspection. But protection of the public health is not a game. It is of vital importance to each and every citizen.[89]

On June 17, 1962, former Secretary Ribicoff said:

> All too often inspectors are treated to a guided tour through the establishment. They are refused access to formula files, complaint files, shipping records, and a great deal more information that is absolutely essential for them to see in order to determine whether products are being produced in compliance with law . . . .
>
> Every working day a food, drug or cosmetic manufacturer refuses to give our inspectors access to information needed to safeguard the public. These refusals are not restricted to the fly-by-night operator but extend to some of the very largest manufacturers in this country. We call upon the Congress to examine this situation.[90]

The Situation Regarding Record Inspection Refusals

At the conclusion of the 1962 hearings the FDA gave some specific examples in which a manufacturer or a processor refused to

---

[88] H. R. Doc. No. 60, 88th Cong., 1st Sess. 7; FOOD DRUG COSMETIC LAW REPORTS, No. 359, February 15, 1963.

[89] *New York Times,* Mar. 16, 1962, p. 16, col. 6.

[90] Hearings on H. R. 11581 and H. R. 11582 Before the House Committee on Interstate and Foreign Commerce, 87th Cong., 2nd Sess. 67 (1962) (hereinafter cited as "1962 Hearings").

provide inspectors access to records which may have had a bearing on a violation of the 1938 Act.[91] In addition the FDA submitted a long list of inspection refusals during the period from January 1, 1962, to June 15, 1962.[92] The list was classified according to the type of refusal:

(1) to permit inspection;
(2) to divulge status or responsibility of individuals;
(3) to furnish qualitative or quantitative formulas;
(4) to disclose or permit observation of manufacturing procedures;
(5) to permit review of complaint files;
(6) to permit taking of photographs;
(7) to permit review of shipping records;
(8) to permit review of control records; and
(9) to permit review of prescription files.

Industry's argument runs that, whenever the government states pressing reasons for seeing confidential records, the vast majority of industries will oblige.[93] In some instances industry has not felt that the FDA inspectors presented proper reasons. To protect itself from what it deemed overzealous enforcement, it has denied access to records as it is legally allowed to do under the 1953 Factory Inspection Amendment.[94]

In presenting a lengthy list of companies refusing to allow record inspection, has the government made a convincing case for taking away the voluntary aspect of record disclosure? The present writer feels that the list by itself is insufficient evidence that new legislation is needed. First of all, refusals to permit general inspection and observation of manufacturing processes are illegal under present law and thus can already be dealt with. As to the other refusals, the FDA did not demonstrate that the information sought had a bearing on a violation of the 1938 Act.

The Question of Consumer Protection

It can be safely assumed that no responsible representative either of government or of industry fails to be interested in the protection of the consumer. Industry cites its general support of the 1953 Inspection Amendment, the 1958 Food Additive Amendment and the

[91] 1962 Hearings 578-581.
[92] 1962 Hearings 589-592.
[93] 1962 Hearings 165.
[94] 1962 Hearings 155.

1960 Color Additive Amendments as evidence of its concern.[95] A major point in its opposition to further extension of the FDA's inspection authority is that the consumer can be adequately protected under provisions of present legislation.

B. G. Habberton, representative of the dairy industry testifying before Congress, gave an answer to the former Secretary Ribicoff's statement of June 19. He stated that if under present laws inspectors were taking "guided tours" of plants and "failing to ascertain the required information concerning possible adulteration or misbranding, it would seem they are not doing their duty. What (would be) required in this situation is not more authority but more exercise of the authority which already exists."[96] He also took sharp issue with the former Secretary's contention that it was necessary "to see the manufacturers' formula files, complaint files, and shipping records in order to determine whether the products are being produced in compliance with the law."[97] On the matter of chemical additives, Habberton maintained that if the FDA makes proper use of the rigorous safeguards built into the 1958 Amendment public safety will be assured.[98]

William W. Goodrich, Assistant General Counsel for the FDA speaking before a group at the American Bar Association Convention on August 8, 1962, did not linger over the subject of extension of the government's jurisdiction in the areas of adulteration and misbranding, but passed on directly to "the paramount problem of the day—the safe use of a multitude of chemicals in our foods."[99] He quoted another portion of former Secretary Ribicoff's statement of June 19 which decried the fact that some industries denied the government access to records regarding the use of food additives. Goodrich expanded Ribicoff's point:

> It is no answer to say that we can observe the manufacturing processes and the raw materials and that we can analyze the end product. First, we cannot maintain a continuous inspection to station an inspector at the point of manufacture each time a food additive is used. Secondly, objective analysis is a very expensive and uncertain way to enforcement.[100]

Since Goodrich is certainly correct in stating that the government cannot undertake full-time supervision of any industry, the

---

[95] 1962 Hearings 132.
[96] 1962 Hearings 437.
[97] 1962 Hearings 438.
[98] 1962 Hearings 439.
[99] Goodrich, Wm. W., "The Case for the Factory Inspection Amendment," 17 Food Drug Cosmetic Law Journal 516, 520 (1962).
[100] Cited at footnote 99 at p. 521.

pertinent question would seem to be: would guaranteed access to industry records give the government a substantially greater degree of assurance than it now has that its regulations were being complied with when its inspectors were not present? The writer is not convinced that it would. Knowing that the government could inspect raw materials and the manufacturing process, and analyze the end product, few firms would want to risk government penalties and unfavorable publicity by knowingly producing an unsafe batch. The few that would take the chance would doubtlessly reduce the risk of disclosure by "adjusting" their records.

Goodrich states that "objective analysis is a very expensive and uncertain way to enforcement."[101] Would examination of subjective records be nearly as certain?

THE DEBATE CONCERNING LEGALITY: CONSTITUTIONAL CONSIDERATIONS

During the legislative hearings prior to the passage of the Drug Amendments of 1962, representatives of industry reiterated a number of their arguments concerning the unconstitutionality of granting the government power to compel industry to reveal its records to government inspectors. The major points made may be summarized as follows:

Industry maintains that the FDA, assured access to a company's files, would be able to engage in a "fishing expedition" or general search for evidence of wrongdoing to be used against the inspected company. The act of forcing a business to reveal its private papers without specific cause, industry states, is a violation of the 4th Amendment, which has been held to protect companies as well as individuals from "unreasonable search and seizure."[102] The use of information acquired by examining such private papers in prosecution constitutes a violation of the 5th Amendment, which prohibits forcing one to give evidence against himself.[103] Moreover, industry argues, the FDA does not need to open itself to these charges of unconstitutionality. There are already methods, having proper safeguards, for compelling disclosure of records which are relevant to a suspected violation.[104]

---

[101] Cited at footnote 99.
[102] 1962 Hearings 138.
[103] 1962 Hearings 539.
[104] 1962 Hearings 563.

Congress was impressed by such arguments to the extent that it removed from the bill the hotly contested phrase giving the FDA power to compel disclosure of records bearing on whether there might be "potential violations." As the law now stands, the FDA's investigatory jurisdiction extends to records bearing on whether there might be "violations." Congress more specifically revealed its intent to limit the FDA's fishing license by excluding financial, sales, pricing, certain personal and certain research data from its view.[105] While making these limitations, Congress demonstrated its general belief in the constitutionality of making record inspection compulsory, so far as the prescription drug industry is concerned, by granting the FDA just such powers.

As a practical matter, even the striking out of the words "potential violation" is for the most part a hollow victory for industry. Elsewhere in the amendment it has been asserted that products not manufactured "in conformity with current good manufacturing processes" are in violation of the Act. It is difficult to see how papers bearing on whether good manufacturing standards were being met would differ from papers bearing on whether there were potential violations.

Will the present record inspection provision hold up in court? An examination of Supreme Court decisions regarding the relation between corporations and the 4th and 5th Amendments reveals that the record inspection provisions will probably not be seriously challenged on constitutional grounds.

As early as 1906 the Court stated its view that the 5th Amendment had nothing to do with corporations in *Hale v. Henkel.* Its line of reasoning ran that corporations, created by the government and endowed by it with both privileges and duties, do not possess the individual's right to withhold evidence against himself.

> It would be a strange anomaly to hold that a State, having chartered a corporation to make use of certain franchises, could not in the exercise of its sovereignty inquire how those franchises had been employed, and whether they had been abused, and demand the production of the corporate books and papers for that purpose.[106]

This same case provided specific comment on the relation of the 4th Amendment to protection of corporations from governmental record inspection. "We do not wish to be understood as holding that an examination of the books of a corporation, if duly authorized by

[105] 21 U. S. C. A. Sec. 374(a) (Supp., 1962) as amended; FOOD DRUG COSMETIC LAW REPORTS ¶ 2661.

[106] *Hale v. Henkel,* 201 U. S. 43, 74-75 (1906).

act of Congress, would constitute an unreasonable search and seizure within the 4th Amendment."[107]

More recent opinions, such as those in *Fleming v. Montgomery Ward* (1940) and *United States v. Morton Salt* (1950), do not shirk from the authorization of "fishing expeditions" by regulatory agencies. Government inspectors should be assured access to business records "regardless of whether there is any pre-existing probable cause for believing that there has been a violation of the law."[108] An administrative agency has powers analogous to those of a Grand Jury, "which does not depend upon a case or controversy for power to get evidence but can investigate merely on suspicion that the law is being violated or just because it wants assurance that it is not."[109]

Further evidence that the wording of the new Drug Amendments regarding record inspection is not liable to be challenged by the courts consists of the fact that a governmental agency similar to the FDA, the Federal Trade Commission, has been imbued with such powers since 1914.[110]

THE DEBATE REGARDING POSSIBLE NEGATIVE RESULTS

In addition to its questions regarding need and legality, industry has raised the problem of whether undesirable side effects might result from the extension of governmental record inspection authority.

Effect on Industry's Maintenance of Records

Throughout the 1962 hearings, industry representatives stated their proposition that a law assuring governmental access to corporation records would decrease rather than increase consumer protection. Legitimate companies, the argument ran, would be apt to cease recording certain negative information, which, though valuable in maintaining high standards, might invite misinterpretation, unfavorable publicity, or prosecution. The position was stated succinctly by Frank T. Dierson, General Counsel for Grocery Manufacturers of America.

The keeping of accurate records relating to manufacturing processes, quality controls, consumer complaints, personal qualifications, etc., is a voluntary

[107] Cited at footnote 106.

[108] *Fleming v. Montgomery Ward & Company,* 114 F. 2d 384, 390 (CA-7 1940), cert. denied, 311 U. S. 690 (1940).

[109] *United States v. Morton Salt Company,* 338 U. S. 632, 642, 643 (1950).

[110] Mueller, Charles E., "Access to Corporate Papers Under the FTC Act," 11 *Kansas Law Review* 77 (1962).

practice normally and faithfully observed by the food manufacturer. He follows these procedures in order to maintain and improve the quality of his product, to correct any deficiencies as quickly as he can discover them, and by experience and training to develop the finest professional staff to conduct skillful research, development, production, and distribution in the field of his food technology. It requires little more than a statement of the food manufacturer's reasons for keeping these records to demonstrate that they indirectly but importantly contribute to the welfare of consumers, and that anything which needlessly discourages the keeping of these records operates to the detriment of the public interest.[111]

Industry made the further point that record inspection would "fail of its purpose because fly-by-night operators who would engage in willful adulteration would not be expected to keep records."[112]

Subsequent to the passage of the 1962 Drug Amendments FDA made its answer to industry's latter point by issuing the proposed regulations making record-keeping compulsory.

The over-all usefulness to the FDA of its new record inspection authority will certainly be enhanced by the twin power it has assumed to compel record-keeping. The new regulations will doubtlessly make "flying-by-night" more difficult. On the other hand, record-keeping in heretofore scrupulous firms may still suffer on account of the new legislation. As the government itself acknowledges in the proposed regulations, its requirements for record-keeping must be along general lines;[113] thus legitimate manufacturers may well decide they can no longer risk maintaining certain specific valuable records which are subject to misinterpretation. The new amendments and regulations regarding the records of the prescription drug industry, then, will probably make it harder for a company to be either illicit or superior.

In light of this issue the advisability of extending the FDA's record inspection authority to cover the food, cosmetic and non-proprietary drug industries may be considered. As the FDA seeks to enforce the Act its first priority is protection of the public's health. Safety is more difficult to assure within the prescription drug than within the other regulated industries. Thus, the fact that record-keeping, record inspection regulations may hinder the corner-cutter assumes great weight even when balanced against the fact that the

[111] 1962 Hearings 608.

[112] 1962 Hearings 645.

[113] Hansen, Douglas C., "Manufacturing Control," Proceedings: FDA Conference on the Kefauver-Harris Drug Amendments and Proposed Regulations, Feb. 15, 1963, 14-15.

legitimate operator may be penalized. When there is less immediate potential for public harm, then the long-range deleterious effects of the regulations take on greater importance. The conclusion may be drawn that extensive record inspection authority for the FDA, insofar as its effect on record maintenance is concerned, is not as valid in regulation of the food, cosmetic and nonproprietary drug as in the prescription drug industry.

Disclosure of Trade Secrets

Industry on many occasions has expressed the further concern that governmental record inspection would lead to the revealing of a company's confidential information. The view was stated at the 1962 Hearings by Franklin M. Depew, Chairman of the Food, Drug, Cosmetic Section, New York Bar Association, as follows:

> It cannot be too strongly stated that inspection of these factories as provided by this section, by outsiders, can expose to the world trade secrets, know-how, and other confidential information. This technology is in the truest sense the property of its owners. Frequently, it constitutes the element of greatest value—in economic and competitive terms in the manufacture of a product. To subject such technology to outside inspection exposes it to possible dedication to the public domain.[114]

When the FDA cites that there are rigid penalties for disclosure of confidential information and that there have been no known instances where disclosure has occurred, industry replies that disclosure is exceedingly difficult to prove, especially when "yesterday's government official (becomes) tomorrow's private employee."[115] Industry is further concerned that, if a trade secret became relevant in a private suit, a subpoena might force its revelation.[116]

There is little doubt that protection of trade secrets is of vast importance to companies within many industries. (A report appeared recently in *The New York Times*[117] stating that the B. F. Goodrich Company is bringing a test case through the courts on the matter of a former employee, who helped develop a secret formula, going to work for a competitor.) Once again this fact assumes weight, in considering the extension of record inspection authority, to the degree that health and safety are not endangered.

---

[114] 1962 Hearings 427.
[115] Cited at footnote 114.
[116] 1962 Hearings 628.
[117] *New York Times,* Western Edition, Mar. 22, 1963, p. 11, col. 4.

CONCLUSION

There is little doubt that it is constitutional to extend the FDA's record inspection authority. The important question as to the wisdom of such extension remains. It would seem that industry's concerns regarding protection both of trade secrets and of the usefulness of its confidential records are real, and that industry's privacy should be respected insofar as danger to public health is relatively insignificant.

Thus within areas of the food, cosmetic and nonproprietary drug industries that do not use toxic substances, on-the-scene observation of manufacturing processes and objective analysis are not only less objectionable to most companies, but more reliable than inspection of written reports in assuring consumer safety. Where toxic substances are used, greater precautions are needed. Nevertheless, inspection of the type used for the prescription-drug industry still does not seem justified, since toxic substances are used in relatively miniscule amounts. Here, the present program under the Food and Color Additive Bills of submitting new products and processes for governmental approval prior to their introduction on the market, combined with objective inspection and analysis by the government after their manufacturing has begun, would seem to be both realistic and relatively inoffensive to industry in safeguarding the public. It would seem logical to extend the use of this procedure to cover cosmetics in which poisonous substances are used.

If the dual criteria of industry protection and public safety is applied, it also seems legitimate to extend governmental authority so that it may compel the disclosure of one type of information. It would be hard to demonstrate that shipping records contained trade secrets or that they were "subject to misinterpretation," but it is easy to see that their disclosure is essential in protecting the consumer when suspect products are being distributed.

In a limited number of specific areas, then, extension of governmental inspection authority seems justifiable. For the most part, however, new laws are not the best means to secure more effective and efficient consumer protection. A better way to achieve the goal is through improvement of working relationships between government and industry.

The Assistant General Counsel for the FDA has asked the question, Why does industry "object to inspection rights by the Food and Drug Administration which stands as a representative of the

consumer[118]"? Perhaps one basic answer is that industry is generally suspicious of the FDA because of its police image. In the past the FDA has shown the tendency of a law enforcement agency to rely upon legal sanctions as its chief mode of operation.

Commissioner Larrick has publicly acknowledged the recommendations made by the Second Citizens Advisory Committee Report on the Food and Drug Administration, which cited three stages of development in a health regulatory agency. They are: "(1) The period of police power enforcement; (2) the period of health education (mutual cooperation); (3) the period of mandated self-inspection and self-regulation." The report held that FDA has been in the first stage so far. "It should proceed to the second and third stages as rapidly as the necessary changes in administrative philosophy can be achieved."[119] Such a change in policy would do much to eliminate responsible industry's resistance to the FDA. Instances in which companies have collaborated with the agency in the planning of new regulatory programs by furnishing valuable recorded data on trade practices would be repeated and multiplied.

In commenting on the Citizens Advisory Report, Commissioner Larrick stated:

> We will always, in my opinion, need to employ the sanctions of the statute to effectuate its purposes, but recent developments . . . have emphasized that administrative actions designed to implement preventative enforcement should be undertaken at an accelerated pace. This we plan to do.[120]

It is hoped that the inevitable emergencies, such as the tuna episode in the Spring of 1963, will not distract the FDA from this goal.[121] **[The End]**

---

[118] Goodrich, cited at footnote 99, p. 522.

[119] The Second Citizens Advisory Committee Report on the Food and Drug Administration, 17 FOOD DRUG COSMETIC LAW JOURNAL 599; FOOD DRUG COSMETIC LAW REPORTS, No. 348, November 2, 1962.

[120] Larrick, Geo. P., "Administering New Food and Drug Laws," 18 FOOD DRUG COSMETIC LAW JOURNAL 133, 134 (1963).

[121] "Tuna Episode Spurs Factory Inspection Bill," *Food Processing,* pp. 23-24 (June, 1963).

"Testifying at the end of April (1963) in the House Public Health and Safety Subcommittee's review hearings on FDA and public health programs of the HEW Department, Food and Drug Commissioner George P. Larrick spoke of thalidomide and tuna fish in a single breath. Mr. Larrick made specific legislative request to the subcommittee, saying in part:

"'The factor inspection authority which was extended and clarified last year with respect to firms manufacturing prescription drugs should be extended and clarified with respect to all other manufacturers of foods, drugs and cosmetics.'"

The Food and Drug Administration's View of Investigational Drugs

By EARL L. MEYERS

Dr. Meyers Is Chief, Controls Evaluation Branch, Division of New Drugs, Bureau of Medicine, of the United States Department of Health, Education and Welfare. The Address Was Delivered at the Annual Pharmacy Congress, St. John's University, New York, April 18, 1963.

IT IS INDEED A PLEASURE to join the distinguished speakers on this panel and participate in this symposium on investigational drugs. It is timely to take a new look at the subject since the recent enactment of the Kefauver-Harris Amendments to the Federal Food, Drug and Cosmetic Act and the promulgation of the investigational drug regulations which became effective February 7, 1963. At no time in this country's history has the private citizen been more interested, more concerned, and more inquiring about drugs and their relation to his health.

Largely due to the tremendous strides in the general field of chemistry over the past two decades, there has been a parallel surge in the pharmaceutical industry, resulting in the greatest development of new drugs ever experienced in any like period of medical history. The increased factory inspection authority and possibly some of the other provisions added to the Food, Drug and Cosmetic Act by the amendments were undoubtedly catalyzed by the thalidomide disaster. The need for such controls had, however, been recognized and plans for meeting this need had been under study for a considerable period prior to this occurrence. The investigational drug regulations represent a crystallization of many years of Food and Drug Administration experience and virtually all of the new concepts contained therein were developed before the thalidomide case. Likewise, the new legislation is mainly derived from more than two years of congressional hearings and legislative recommendations developed before the thalidomide case. Had the same changes been accomplished gradually, their impact would seem less drastic.

Past Data Requirements Inadequate Now

It is obvious that the many scientific advancements made in recent years have made the development of new drugs an ever-changing process. So are the techniques, methods of approach and scientific developments that may reasonably be expected to be performed to demonstrate safety, and now effectiveness, and hence to be reflected in a new drug application. It should be apparent then that the amount and type of data that were considered sufficient 20 or even 10 or 5 years ago to support a new drug application might now be deemed inadequate. In this regard we can no more be static in our requirements than is the manufacturer in his application of new methods to his drug development programs.

Let us first consider the principles under which we now are operating the new drug provisions of the Food, Drug and Cosmetic Act.

Definition of "New Drug"

One of the major changes brought about by the new legislation is in the definition of a "new drug." "Effective" has been added to the definition. The term "new drug" now means any drug which is not generally recognized as safe and effective by experts qualified to evaluate the safety and effectiveness of drugs when used under the conditions prescribed, recommended, or suggested in its labeling, or which is recognized as safe and effective as a result of investigations but has not been used for a material time or to a material extent under such conditions.

The Federal Food, Drug and Cosmetic Act of 1938 prohibited the shipment of a new drug in interstate commerce until the distributor had obtained an effective new drug application for it. The purpose of the preclearance for safety has been to obtain advance proof that the drug would be properly prepared, adequately labeled, and safe for use under the conditions prescribed, recommended, or suggested in its labeling. We have invariably considered efficacy in connection with safety in clearing new drugs when they were for a progressive or life-threatening condition or when they had a significant toxic potential for harm to the patient. Safety is a relative matter with drugs, and effectiveness has been treated as the balancing factor in determining whether a new drug could be permitted to be marketed. But the new drug provisions did not authorize us to control exaggerated claims or to exclude from the market worthless but essentially innocuous products.

Evidence of Effectiveness Required

The Kefauver-Harris Amendments of October 10, 1962, require an approved application not only for the safety of the drug, as previously, but also for effectiveness. New drugs may be excluded from the market or removed from the market when there is a lack of substantial evidence that they will do what is claimed in their labeling. Substantial evidence of effectiveness means adequate and well-controlled investigations, including clinical studies, on the basis of which it can reasonably and responsibly be concluded that the drug will have the effects claimed. Now, manufacturers of new drugs will therefore need to demonstrate their effectiveness as well as safety for the conditions prescribed, recommended, or suggested in their labeling.

For drugs now having an effective new drug application, applicants generally have a two-year transitional period from October 1962, before such drugs could be ordered off the market on the sole ground of lack of substantial evidence of effectiveness for claims made for them by the previously cleared labeling. In this connection applicants should review their labeling claims to determine whether there is substantial evidence in the application to support them. It is recommended that any previously unreported evidence pertinent to the effectiveness of the drug should be submitted at an early date. Unsubstantiated claims for effectiveness can be eliminated by supplementing the new drug application to provide for labeling without these claims, or marketing of the drug may be discontinued with resumption of marketing under the provisions of an approved supplemental application supported by substantial evidence of effectiveness.

In order to obtain data to show safety and effectiveness the drug must be distributed to investigators. Accordingly, the statute includes a provision which allows such distribution and authorizes the Secretary to issue regulations in this connection. Regulations under which we had been operating required only that a new drug distributed for investigational use be labeled "Caution: New Drug—Limited by Federal (or United States) law to investigational use," and that the sponsor before shipping such drug obtain from the investigator a written commitment that he would use the drug only for investigation and that he had adequate facilities for this purpose. These statements and records of shipment were subject to inspection by the FDA.

Experience showed that stronger regulations were needed, fortified with concepts designed to maintain better control over the dis-

tribution of drugs not yet proven safe and to guard against abuses which occurred under the existing rules. On August 10, 1962, we published proposed regulations covering these new concepts and designed to correct the deficiencies. Our proposals were subjected to a great deal of helpful and constructive comment by the scientific community. Their objective was rather universally accepted but exception was taken to some of the procedures and protocols. The recently enacted drug amendments require that several specific factors be considered before we exempt new drugs for investigational use. After careful review of all of the submitted comments and after a number of meetings with groups of scientists and others, the final regulations were published on January 8, 1963. They became effective on February 7, 1963.

Intent of the Regulations

The intent both of the regulations and of the law is to ensure, among other things, that the pharmaceutical manufacturer who wishes to have his product tested on man will conduct adequate preliminary studies to justify clinical testing, and will make the results of these tests fully available to the expert investigator and to the government before the drug is administered to man. The manufacturer will have to develop a scientifically sound program for the clinical tests he proposes. He will have to see to it that the new drug is turned over to qualified investigators who will test it on patients under their personal supervision or under the supervision of qualified investigators responsible to them.

It is important to emphasize that a new drug has a different meaning than before passage of the Kefauver-Harris Amendments In other words the investigational drug requirements apply to the clinical study of any drug not generally recognized as effective as well as safe for the intended use.

Important Provisions of Investigational Drug Regulations

Let us consider some of the more important provisions of the investigational drug regulations. Prior to distribution of a new drug for clinical testing in man the sponsor of the investigation is required to submit to the FDA certain specified information as part of a "Notice of Claimed Investigational Exemption for a New Drug." This includes:

(1) The name, dosage form, components, quantitative composition, and the chemical structure, if known, of the new drug substance.

(2) A description of the source and preparation of any new drug substances and the methods used to ensure the identity and uniformity of the new drug. The complex chemistry involved in the synthesis of new drugs, and the information derived from newer techniques in analytical procedures indicate the need for a more detailed description of the synthesis and the specifications for the new drug substance, and reliable tests for the drug as used in its investigational dosage form. These should be incorporated as part of the necessary information in a sponsor's statement.

(3) The methods, facilities, and controls used for the manufacturing, processing, and packing of the new drug to establish and maintain appropriate standards of identity, strength, quality, and purity for safety and to give significance to the clinical investigations made with the drug.

The new drug substance in a dosage form of a drug is probably not the sole determinant of its pharmacological effectiveness. The physiological response may be a function of the formulation of the dosage form as well as the new drug component. The rate at which the amount of the new drug component in the dosage form is physiologically available to the patient upon administration is an important consideration. We have encountered cases of varied clinical response between batches of the same pharmaceutical formulation. Additional study has indicated that differences in physical and chemical properties were caused, among other things, by differences in physical properties of the raw materials such as crystalline or amorphous form and particle size, conditions encountered during processing, and contact of the components in the dosage form resulting in complexing, binding, and adsorption. Therefore, early consideration of these factors during the investigational stages of the drug is necessary.

It also becomes important to establish the reproducibility of the dosage form of a drug from batch to batch if the clinical studies are not to be biased by an unknown variable. All batches must be uniform in identity, strength and quality so that the patient receives what he's supposed to be getting. We have only to recall recent observations that there exists a considerable lack of homogeneity between tablets from the same batch to realize the importance of early work necessary to produce a uniform dosage form of the drug from batch to batch.

The investigational evidence that a drug is safe and effective in use does not necessarily establish that its deterioration products

are safe and effective. Evidence establishing the safety and effectiveness of one or more batches of a new drug under investigation has no significance with respect to the safety of subsequent batches of the drug unless they can be shown to be the same as to identity, strength, quality, and purity as the batches studied. The requirement in the law and regulations that the methods, facilities, and controls employed are adequate to preserve the characteristics of a new drug necessitate study of the stability of the preparation during the investigational stage.

Adequate Information on Preclinical Testing

(4) Adequate information on preclinical testing to show that it is reasonably safe to initiate the proposed clinical studies. This requirement arises from the obvious need to conduct adequate testing on animals before starting human trials. The sponsor's submission should contain detailed data derived from appropriate animal experiments in which the methods used and the results obtained are clearly set forth. This usually means pharmacologic studies in animals. The kind and the amount of information required will depend on several factors, such as the nature of the drug and its indication, and must be determined individually for each new drug.

(5) The labeling or other information to be furnished to investigators. The clinical investigator must have sound information as to prior tests to make his decisions about dosages to employ and hazards and side effects to look for in clinical studies.

Qualifications of Experts

(6) The name and a summary of the training and experience of each investigator or expert. Neither the 1938 law, the new legislation, nor the investigational drug regulations define who is an "expert qualified by scientific training and experience to investigate the safety of drugs." We believe that at least in the early phases of clinical investigation of a novel drug it refers to physicians who have experience in drug investigation and are specialists in the field applicable to the specific drug. Furthermore, they should have adequate facilities for investigation with respect to patients, clinical laboratory services, and time to give attention to such studies. This usually does not apply to the busy general practitioner. Initially, the anticipated effects of the sections of the regulations dealing with the qualifications of experts are that sponsors of investigations will obtain

and more carefully consider the qualifications of investigators to do what is required with safety and in a manner that will contribute to an evaluation of the drug. Clearly, a clinical investigator should be qualified, should maintain and make available required records and reports, and should use sound scientific judgment in testing a new drug. The information with respect to the qualifications of investigators will be helpful to the FDA in evaluation of their reports in new drug applications.

(7) An outline of the planned investigations, which may be submitted by phases. Phases (1) and (2) cover the clinical pharmacology with administration of the drug in a closely controlled scientific environment to a limited number of patients and under professional controls which assume a large measure of safety. Phase (3) covers the clinical trial in which the drug is used with a larger group of patients by different physicians following substantially the same investigational procedures. Reasonable flexibility of a plan of investigation is provided for. An investigator may pursue promising leads that may emerge in the early stages of his investigations, and he may modify experimental design on the basis of experience, advising the sponsor in progress reports. During clinical studies, reasonable variations of investigators, patients, and design are possible.

(8) If the drug is sold, a full explanation of why sale is necessary. In certain instances there may be justification for charging for an investigational drug. However, we believe we should have the facts so that we may reach our own decision as to whether sale of the drug represents premature commercialization.

The regulations also provide that neither the sponsor nor any person acting on his behalf shall disseminate any promotional material representing the investigational drug to be safe or useful for the purposes for which it is under investigation. In consideration of this point in the regulations, fear was expressed that this would prevent the presentation or publication of scientific papers or reporting of such in the lay press. This is definitely not its intention. Nothing here would foreclose an exchange of scientific views about a new drug by scientists. Nor would anything here interfere with bona fide science reporting.

The sponsor also is required to inform all investigators and the FDA of findings which suggest any hazard in use of the drug, and to discontinue the investigation and to recall outstanding stocks of

the drug if the investigations reveal facts showing that there is substantial doubt they may be continued safely. The prompt dissemination of findings of adverse effects may facilitate their early evaluation which would not otherwise occur if they remained as isolated observations, possibly without identification of the drug as a causative agent.

It should also be noted that when the sponsor files with the FDA the notice of claimed investigational exemption for a new drug, he and the investigators are free to proceed without notification. If, however, there is failure to comply with the conditions of the exemptions and failure to correct the situation on notification of it, the Commissioner shall notify the sponsor of the termination of the exemption.

Reports from Investigator to Sponsor

Each investigator involved in clinical pharmacology and in clinical trials is required to submit the following information to the sponsor of the investigation:

(1) A statement of his education, experience, and the facilities he will employ in the investigation.

(2) An outline of the plan for his investigation.

(3) Statements showing he understands the conditions governing the use of investigational drugs, including the maintenance of records, the submission of reports to the sponsor, and making his records available for government inspection.

Some investigators have felt no obligation to submit reports and some sponsors have exerted little effort to obtain them. Making the submission of reports a condition for receiving the drug should go far in correcting this. We have received a number of comments to the effect that the burden of producing required records and reports will discourage some physicians from participating in investigations. This may well happen in some instances. However, the failure to record and report results of the investigational use of drugs for the benefit of the medical community may lead to a repetition of drug injuries and deaths that may otherwise be avoided.

We have also received comments with respect to the provision which allows inspection of the records of the investigators in that this may encroach on the physician-patient relationship. There is no intent to require individual patient identification ordinarily. Such

information may be considered necessary, however, in certain instances where there is reason to believe that the records do not represent actual cases studied or do not represent actual results obtained or where the records of particular patients indicate that a more detailed study is required.

Patient Consent Provision

Of particular interest is the patient consent provision included in the new amendments to the Act. It is required that the sponsor of the investigation obtain a certification from an investigator that he will inform any human beings or their representatives (including controls) that the drug is being used for investigational purposes and obtain their consent for such use except where the investigator deems it not feasible or, in his professional judgment, contrary to the best interests of such human beings. This requirement reflects the long-standing belief by our society and others that patients who are being used as experimental subjects should first give their consent.

We received a number of comments with respect to the special status of radioactive new drugs for investigational use. Pending further consideration, these drugs are exempt from the investigational drug regulations if they are shipped in accordance with current regulations of the Atomic Energy Commission.

The investigational drug regulations contain only a brief statement on new veterinary drugs for investigational use pending issuance of specific regulations. The regulations provide for use of drugs for tests on animals. However, meat, milk and eggs derived from treated food animals may not be used for food purposes until the FDA allows such use on a showing that drug residues do not cause the food to be unsafe.

Final Regulations Not Immutable

Final regulations are not as immutable as the word "final" may imply to the nonbureaucrat. The investigational drug regulations can be changed when the need for change becomes apparent. The medical profession, pharmacists, pharmaceutical manufacturers, and any others who are interested should feel free to suggest improvements at any time. And where such suggestions are consistent with our joint basic responsibility to see that the rights of patients are fully safeguarded in a testing program, we will propose appropriate changes.

Such proposals would be subject to comment by interested persons just as the current regulations were.

We anticipate that the sponsor's statement on investigational antibiotic drugs will be processed by the same scientists as any other investigational drug. All of the scientific and technical resources of the FDA will be employed in the evaluation of the sponsor's notice and of the progress reports.

Where drugs were under clinical trial on man on or after August 10, 1962, the sponsor was required to submit a list of such investigational drugs by March 9, 1963. We have received lists containing the names of approximately 2,500 drugs which were under investigation. The sponsor is required to submit to the FDA by June 7, 1963, the completed "Notice of Claimed Investigational Exemption for a New Drug," a new drug application, or a statement of discontinuance of clinical trials for each of these listed drugs.

If a sponsor proposes to continue the clinical investigation of his drug after he submits a new drug application, it will be necessary for him to submit a completed "Notice of Claimed Investigational Exemption for a New Drug," or to furnish all the information required by such "Notice" covering the continuation of the clinical trials as part of the new drug application. Any information already a part of the new drug application may be incorporated by reference in a sponsor's statement.

After an application is approved it may be desirable to initiate additional investigations with the drug. If such investigations are limited to use of the drug under conditions covered by the approved labeling as to indications, dosages, duration, and so forth, then no advance notification to the FDA is required. An example of such studies might be double blind comparison of the approved dosage form of the new drug with a placebo and other active drugs to develop additional information with respect to effectiveness. Although no prior notification is required, the results of such studies should be reported to the FDA under the records and reports requirement for approved drugs and antibiotics contained in the Kefauver-Harris Amendments.

However, if the clinical investigations involve use of the drug for purposes or under conditions as to indications, dosage, or duration of use differing from the approved labeling, prior to starting clinical study, it should be covered by submission to the FDA of the claimed

investigation exemption to the extent applicable. Data required by the sponsor's statement may be incorporated by reference to the approved new drug application.

The marvelous advances that have been made in recent years by most firms to improve the new drug supply must be carried forward. Firms that carry out these investigational procedures in their own facilities must assure themselves of the competence and reliability of scientific personnel in charge of this work. They must further provide the scientists with complete and up-to-date equipment, adequate to maintain the identity, strength, quality and purity of such new drugs. Those firms which rely upon independent laboratories must assure themselves that the laboratory they choose is reliably fulfilling the tasks it has agreed to perform.

Start of a New and Challenging Period

No doubt every one of us will agree that the past year has marked the start of a new and challenging period for the drug industry. A combination of circumstances has aroused the public interest in knowing more about the drug business. There is no doubt in my mind that the operations of the FDA will be subjected to the same close scrutiny as the operations of the drug industry.

The government regulatory official must always remember that the work he is doing and the decisions he is making are subject at any time to public review. And it may well be that the only way the drug industry is going to keep the confidence of the American public in its products will be for it to live in a goldfish bowl, too.

Whenever in the past there have been new controls proposed for the drug industry and for a time after new legislative controls came into force, there were numerous voices heard decrying the ruin of this industry. It is no different at this time. It should be emphasized that the investigational drug regulations are designed to eliminate all unnecessary risks to the public that may arise from the development of new drugs and at the same time to impose only those restrictions on the conduct of investigational procedures necessary to accomplish this.

Conclusion

The regulations establish no criteria as to what constitutes adequate preclinical investigation to justify tests in man. We will deal with gross inadequacies initially. We propose to utilize fully the

resources of the medical and scientifically related communities, including the competent scientists in industry, to develop criteria that in the long run will raise standards to further minimize the risks inherent in new drug development. It is not our purpose to interfere with the development of useful new drugs but to promote a responsible approach utilizing the best available methodology.

We have discussed some problems relating to investigational drugs. It is not possible in a limited time to discuss all of the aspects of the problem. I, for one, believe we cannot reasonably furnish a blueprint for a general plan of investigational studies of new drugs. I believe, however, that scientists, whether they are from industry or government, can easily agree as to the adequacy of any particular study and what constitutes a reasonable interpretation of its results. I am sure we will agree that the public health and a safe and effective drug supply are the first considerations. **[The End]**

ANNOUNCE STUDY OF STATE AND LOCAL FOOD AND DRUG LAWS

Food and Drug Administration Commissioner George P. Larrick has annouced that a comprehensive study of state and local food and drug laws and their enforcement will be conducted. The study of state and local food, drug, device, cosmetic, and hazardous substances laws, programs and facilities has the following basic objectives:

1. To identify what the state and local governments are providing consumers in terms of food and drug protection.

2. To identify and analyze similarities, variations, inconsistencies, and duplications affecting the laws, workload, organization, personnel, facilities, program, policies, budgetary and other problems confronting state and local agencies.

3. To identify areas which could be improved by better state and local laws, organization, personnel, facilities, programs, policies, budgets and federal programs, or by improved coordination between federal, state, and local programs, and provide recommendations to accomplish improvements in each identified area.

4. To provide goals, guidelines as to means of approach, and timetables to attain any improvements and modifications deemed necessary.

Commissioner Larrick advised that it is hoped that the independent study by an organization outside of government will bring to light any needed improvement in laws, organization, and support for federal-state coordination.

Public Administration Service, Chicago, Illinois, a nonprofit organization, will carry out the project over a period of 18 months. The cost to the federal government will be $250,000.

Liability: Use of Investigational Drugs

By GEORGE E. SCHREINER, M. D.

Dr. Schreiner Is a Professor of Medicine at the Georgetown University Hospital and School of Medicine, and Director of the Hospital's Clinical Study Unit. He Is the President of the American Federation for Clinical Research. This Paper Is Reprinted from the **Proceedings of the National Medicolegal Symposium**, Sponsored by the American Medical Association. The Meeting Was Held in Miami Beach, Florida, March 8-9, 1963.

RECENT DEVELOPMENTS including the growth of clinical research centers, the new FDA regulations and the publicity on Thalidomide have prompted this examination of the moral and legal entanglements of clinical investigation.

Purpose of the Clinical Investigator

The primary purpose of clinical investigation is to produce scientifically reliable data within the framework of a rational experimental design, conceived to answer a specific question, or simply to serve the investigator's curiosity. Experimental design is usually directed toward a significant biology problem. The purpose of drug investigation is to acquire and interpret reliable data which may lead to the proper application of new therapeutic agents. Medicine needs both clinical, basic and therapeutic investigation if it is to advance in knowledge and wisdom.

The purpose of clinical research is not necessarily to remain safe, to please lawyers, to satisfy bureaucrats, to avoid controversy, or even to avoid lawsuits. One can avoid them by not doing clinical investigation.

While fulfilling his purpose, the clinical investigator must work within a framework which includes the personal tastes of the patient, the obligations imposed by the common good, the workings of some fundamental moral code, the times and customs of the society in which the work is to be done, the ethics of the medical profession and the personality and integrity of the investigator.

The purpose of law in this area and, therefore, all the lawmakers and the judges, is to encourage the greatest amount and quality of clinical research which can be done within this framework and to help both the investigator and the patient over apparent conflicts. The law must be forward-looking and constructive. It should not prohibit long lists of specific activities, presume dishonesty on the part of the investigator, police the details of experimentation, or provide a series of legalistic blockades so intricate that the path of progress becomes an obstacle course.

Role of the Clinical Investigator

Possessing, as he does, an unusual degree of drive, a variety of motivating influences and an abiding intellectual curiosity, the clinical investigator is understandably anxious to get on with the job of procuring and interpreting scientifically acceptable data, yet he must at no time lose sight of his parascientific or social obligations.

These include:

(1) The part of his activities which touches directly on the doctor-patient relationship;

(2) The necessity (for the sake of his own long-term interest as well as those of his profession and his contemporary society) of conscious re-affirmation of the dignity of the individual who is acting as an experimental subject; and

(3) The moral implications of a breach of ethics or totally nonconforming behavior even if such actions should result in scientifically acceptable data.

Put in the rather concise and concrete terms of Teddy Roosevelt, "Your right to swing ends where my chin begins." The scientific investigator, while quite legitimately crying for freedom of activity, must in the same breath admit that no freedom of concrete activity can be totally unrestricted.

The Nature of Human Experimentation

One source of confusion in discussions on this topic involves a clear understanding of the nature of clinical research and the patient. The legal precedents which have been well-defined by Ladimer[1] stem from the allegedly negligent application of experimentation to a pure

[1] Ladimer, I. "Experimentation. Medical Practice or Malpractice." *World Medical Journal*, May 1962.

service situation, the giving of a medicine, and operation or a therapeutic maneuver intended solely for the patient's immediate benefit. On the other hand, much of the intellectual writing and legal ruminations has stemmed from public revulsion to the brutal manipulations of human beings carried out by Nazi scientists and documented at the Nuremberg trials. These articles are usually equipped with the slogan "human beings were used as guinea pigs." Actually I know of no instances in which guinea pigs have been so treated. History provides sufficient examples for the summary statement that man's inhumanity to man has far outstripped any brutality encountered in animal experimentation.

The Nature of Human Research

Human research is a spectrum with a decreasing order of direct and personal good to the research subject. Each experiment, the danger of every procedure and the toxicity of a new drug must be examined by the investigator in relationship to such a grading of direct and personal good.

Grade I.—The clinical investigation is concerned in whole or in part with the relative efficacy of a therapeutic regime applicable to the immediate clinical situation of the patient. A concrete example would be the study of a new diuretic agent, a combination of diuretics or a synergism of some physiologic aberration such as acidosis in a patient with refractory congestive heart failure. An efficacious diuretic regime would clearly be beneficial. Here the gravity of the situation determines the limits of acceptable danger and toxicity. The usual example, cancer chemotherapy in metastatic carcinoma, permits the use of highly toxic agents because of the gravity of the prognosis. In the edema problem, one would probably not be justified in using a highly toxic agent nor, on the other hand, be compelled to use agents in the order of decreasing toxicity. One does need to be concerned with the design of the study to yield the proper information.

Grade II.—The investigation might redound to the long-term benefit of the patient, that is they are related to the condition which the patient is actually suspected of having. For example, cardiac catheterization to determine the hemodynamics in the early stages of rheumatic heart disease can be well-justified if it helps to elucidate the natural history of rheumatic heart disease, since at some stage of the patient's known disease he might conceivably benefit from the total body of such information. By the same token, Dr. Gold's ex-

periments on the use of humans for the bio-assay of digitalis preparations would fall into this category.

Grade III.—The use of humans for study or experimentation on conditions which the individual may acquire with a high degree of probability. Examples would be base line studies on young married women who might be expected to become pregnant; research on the common cold; human experiment on the mechanism of auto accident injuries, and so forth. Obviously, all of us would qualify in experiments on arteriosclerosis.

Grade IV.—Human experimentation for conditions which the research subject will not probably acquire. Here justification must bring in some other principle than direct good, such as a contribution to the common good or to society in general. An example would be deliberately induced nutritional deficiencies in human volunteers, deliberate induction of rare diseases or the giving of a disease to a volunteer in a nonendemic area. It is improbable that the knowledge would ever be to his personal good.

Grade V.—Would be the simple use of human volunteers for studies which do not bear any close relationship to any disease process or condition which could conceivably affect them now or later, but which is designed merely to turn up statistical data, biochemical or physical data which might add to the sum total of our basic knowledge. Pure examples are hard to cite. A possible one would be the insertion of needle probes into various organs to measure oxygen tension of normal organs.

It seems to me that these grades of human research require careful, philosophic, legal and moral distinctions. Failure to make such distinctions in our discussion would lead to a great deal of muddled thinking when one has to consider such concrete items as informed consent, pre-clinical animal studies, detailed knowledge of toxicity, ethical rights of domain over our bodies and a host of other considerations. For example, a patient with a crush syndrome might legitimately volunteer for an experimental technique of leg amputation, with the chance that it could also remove a source of infection, catabolism and toxic potassium accumulation. A normal volunteer, however, could not submit to such an operation if our moral code denies him the right to maim or destroy his body.

The Investigator and His Personal Code

In the early experience with human research, the average investigator rarely makes a conscious basic decision concerning the

moral restrictions on his life's work. In the 17 years since I did my first research on a human, including five years as a national officer of the largest organization of clinical investigators, I have encountered at most a dozen individuals who have exhibited skepticism and attempted rationally to dissolve their doubts. For my own students or fellows in that position, I have borrowed a device from Dr. Louis Welt and asked them to read a year's issue of the *Journal of Clinical Investigation,* analyze the experimental design and make a moral judgment as to whether they could do the studies. They have found individual protocols which deviate from their own personal moral code, but I have never encountered a potential investigator who rejected a career in clinical investigation on serious moral grounds. I feel sure that many men resolve their doubts privately, but most investigators, I believe, creep into the moral problems after a series of personal experiences which lead them away from Grade I research into less direct categories where doubt may suddenly assail them. Ultimately one makes his decision on the basis of a personal moral code, his measuring instrument. What are the general codes by which he can calibrate and judge his own instrument? Briefly they are:

The Moral Law.—For the theist this involves considerations of the relationship of man to his creator and his fellow creatures. This has been interpreted in the natural order largely by scholastic philosophers and by the writing or teachings of accepted religious leaders such as the oft-quoted statement of Pope Pius XII[2] in which the moral law is stated "to set up its limits to the medical interests of the patient." This view restricts the patient's right to "involve his physical or psychic integrity in medical experiments or research when they entail serious destruction, mutilation, wound or perils." Such restrictions also impair the right of an experimenter to use himself as the subject.

For the nontheist, moral laws do not have upper case values and obtain their validity by the general agreement of man's experiences, the conscious acceptance of profound leaders, the test of history or the interpretation by natural philosophers of man's dignity as an individual, for example, that of Kant "every man is to be respected as an absolute end in himself . . . it is a crime against the dignity that belongs to him as a human being, to use him as a mere means for

[2] Pope Pius XII. "Moral Limits of Medical Research and Treatment." Read before the First International Congress on Histopathology of the Nervous System, September 14, 1952.

some external purpose." Einstein[3] has summarized this validity in "Out of My Later Years": "It is a privilege of man's moral genius to advance ethical axioms which are so comprehensive, so well founded, that men will accept them as grounded in the vast mass of their individual emotional experiences. . . . Truth is what stands the test of experience."

The Nuremberg Code.—This is summarized below.

"THE NUREMBERG CODE FOR HUMAN EXPERIMENT"

(1) The voluntary consent of the human subject is absolutely essential.

(2) The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

(3) The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problems under study that the anticipated results will justify the performance of the experiment.

(4) The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

(5) No experiment should be conducted where there is a prior reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

(6) The degree of risk to be taken should never exceed that to be taken by the humanitarian importance of the problem to be solved by the experiment.

(7) Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability or death.

(8) The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

(9) During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

---

[3] Einstein, A. "Out of My Later Years." New York Philosophical Library (1950).

(10) During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability or death of the experimental subject.[4]

The personal codes of scientists with a philosophical talent and a highly developed ethical sense.—These are beautifully summarized by Greiner[5] and have reached practical expression in a number of cogent systems.[6, 7]

The code of the American Medical Association.—This is the most concisely expressed code and, in summary, provides:

(1) The voluntary consent of the person on whom the experiment is to be performed must be obtained.

(2) The danger of each experiment must have been previously investigated by animal experimentation.

(3) The experiment must be performed under proper medical protection and management.

A too literal interpretation of the second requirement would, of course, eliminate a major body of valuable clinical investigation. This code has been expanded and is perhaps the most practical set of guidelines currently available for the young investigator. These guides are contained in the report to the Committee on Research and the Council on Drugs of the American Medical Association.[8]

General Background

Study of relevant publications to avoid unnecessary repetitions of experiments;

The physicians conducting experiments should have special knowledge of the problem and be completely responsible;

Good organization and execution;

Every available aid for special or emergency treatment of the experimental subject should be available.

Research Planning

Can the experiment, wholly or partly, be carried out on animals?

---

[4] Nuremberg Military Tribunals, Trials of War Criminals ("The Medical Case") 2:181-184, United States Government Printing Office (1947).

[5] Greiner, T. "The Ethics of Drug Research on Human Subjects." 2 *Journal New Drugs* 7 (1962).

[6] O'Donnell, T. J. "Morals and Medicine." Newman Press, Westminister, Maryland (1956).

[7] Leake, C. D. and Romanell, P. "Can We Agree? A Scientist and a Philosopher Argue about Ethics." University of Texas Press, Austin, Texas (1950).

[8] Beecher, H. K. "Experimentation and Report to the Council on Drugs." 169 *Journal of the American Medical Association* 461-478 (1959).

What is the minimum requirement to obtain the observation? Are its importance and durations ethically justifiable?

What is the minimum requirement in altering the conditions of the experiment?

Are the requirements for the observation and the alterations of conditions the same?

What arrangements are planned? Is the project the fruit of mature thought and expert advice?

How will the results be used in obtaining a definite conclusion?

Risk to Patient

The investigator's responsibility is more important than the willingness of the subject to accept the conditions;

The investigator should consult other experts on the research project in order to intensify the sense of responsibility;

The subject must be fully informed and must consent freely;

If considerable risk is involved, the experiment is not in accord with the object and purpose of medicine;

A practicing physician should not become an investigator on his own patient, if the experiment involves danger. A body of advisers should be consulted.

Experiments should be discontinued if the subject so desires or if unexpected danger is encountered, activities the consequences of which cannot be undone, and which therefore cannot be discontinued, and therefore disapproved;

Any suffering or danger not strictly inevitable must be prevented;

Experiments on children; in institutions for children, old people, etc.; on the insane; or on prisoners, which involve dangerous risks, inconvenience or pain are not approved. All experiments on the dying under any circumstances are disapproved;

The "utmost restraint" must be exercised in experiments on patients deemed to have an incurable malady, even though they volunteer as subjects;

Unnecessary examinations should be avoided, and diagnostic activities that may be dangerous are justified only if they result in effective therapy. In routine examinations new methods that are dangerous should be strictly limited.

The Investigator and Liability

The clinical investigator has truly been in a legal limbo. This situation has been amply summarized by Ladimer.[9] He views legal decisions and precedents on experimentation as not applying to clearly formulated or planned medical research on humans. "There is no case directly prescribing such research and there are no regulatory statutes or legal codes." Ladimer denies that the Nuremberg tribunals have created a legal precedent.[10]

The clinical investigator has, therefore, felt relative legal freedom once he has made a decision which is in keeping with his personal moral code, reinforced by the codes of others. This feeling of security

[9] Work cited at footnote 1.

[10] Ladimer, I. "Ethical and Legal Aspects of Medical Research on Human Beings." 3 *Journal Public Law* 467-511 (1954).

has been buttressed by the fact that he generally works in the protective environment of a university, research institute or hospital. He has a chance to discuss and submit his experimental designs to his colleagues. In effect this is an advance review by a "jury of his peers." Many institutions now have devices for sharing responsibilities such as research committees, or committees on new drugs. Virtually all institutions have administrative echelons which require approval for human research from division or department heads, deans, and so forth. Most medical schools are particularly cautious about the use of medical students as normal volunteers. Administrators of research institutions, schools and hospitals are particularly cautious about experimentation in these special groups:

Types of Research Subjects Requiring Special Caution

1. Children and minors;
2. Patients with psychiatric diagnoses;
3. Investigators, laboratory personnel and medical students;
4. Civil prisoners;
5. Inmates of orphanages, asylumns and corrective homes; and
6. Volunteer religious groups, for example, conscientious objectors and Mennonites.

These considerations are well summarized in the National Institute of Health booklet on the use of normal volunteers.[11]

This relative security of the clinical investigator has been disrupted of late by three main events:

(1) The rapid growth of clinical research centers sponsored by the NIH in a large number of medical institutions which has had the effect of making research volunteers economically feasible outside the intramural program which previously existed in the NIH and other research institutes. Happily for the investigator this program has grown to wide acceptability without a clear statement on the part of the National Institute of Health as to their legal liability for the natural health consequences, for contestable consequences, for admitted mistakes or for the consequences of negligence in human research.

The third-party agents in medical care such as the health insurance plans have not clearly accepted liability for accidents, mistakes or even inter-current illnesses during the course of an experimenta-

[11] "Handbook on Utilization of Normal Volunteers in the Clinical Center." National Institute of Health, January, 1961.

tion. Moreover, many hospitals and institution insurance carriers have implied a denial of responsibility except in the case of litigated malpractice.

(2) The recent regulations proposed by the Food and Drug Administration which provide for the first time a specific body of technical directions to which the investigator is subject.[12]

Time does not permit full exposition of these requirements but they include necessity for written certification by the investigator of "adequate" education and training qualifications, access to research facilities, a general outline of the project, full information on pre-clinical investigation, full records on drug disposition, maintenance of all records for two years, "personal" supervision of the research, responsibility for informed consent and even a divulging of the names of the subjects if "the records of the particular subjects require a more detailed study of the cases or . . . there is reason to believe the records do not represent actual case studies."

The consent provision has fortunately been modified to permit double blind studies, investigation of psychic or emotional phenomena and habituation and research on patients whose diagnoses may not be prudently divulged. This loophole was provided in the provision, "The investigator will certify that he will inform any patients or any persons used as controls, or their representatives, that drugs are being used for investigational purposes, and will obtain the consent of the subjects, or their representatives, *except where this is not feasible or, in the investigator's professional judgment,* is contrary to the best interest of the subjects." While the exception thus provided is broad, the intent of informed consent is clearly stated. At this point no investigator can know how the courts will accept the exception.

(3) The Thalidomide disaster and the rash of emotional writing which has been its consequence.

This, for the first time, has exposed to the public some of the details of poor clinical investigation and has raised their index of suspicion. It also has created a wave of anti-intellectualism and will undoubtedly make future research subjects suit-conscious. Coupled with the series of technical requirements contained in the Food and Drug Regulations, lawyers representing patients who are involved in research projects have a tangible check-list with which to judge the clinical investigator.

---

[12] *Federal Register,* pp. 179-183, January 8, 1963.

Summary

The primary purpose of clinical investigations is scientifically reliable data. A clinical investigator walks where others fear to tread, works in a difficult area and must take full responsibility for his professional decisions as well as full recognition of his parascientific obligations, including those to the patient, his profession, to society, to his personal philosophy, and to his code of ethics. Danger of new drugs or experimental procedures is best judged not by considering it against human research in general, but by the grades of human research which have been related to the directness of personal good. Many more guidelines are available and most reasonable clinical investigators in contemporary society can probably develop a personal code which is in general agreement to such widely accepted forms as the moral law, Nuremberg code and the ethical principles of the American Medical Association. Recent developments have strikingly increased the practical legal problems of the clinical investigator. These have included growth of clinical research center facilities, regulations of the Food and Drug Administration and the public reaction to publicity on Thalidomide. The clinical investigator, once in a legal limbo, is now out on a legal limb. **[The End]**

ANNOUNCE RECIPIENTS OF AOAC WILEY AWARD

Recipients of the 1963 Harvey W. Wiley Award of the Association of Official Agricultural Chemists were recently announced. The $500 award is presented annually for outstanding contributions to the development of methods for the analysis of foods, drugs, cosmetics, feeds, fertilizers, pesticides, or for use in general analytical chemistry. The award was established in 1956 to honor the father of the original Pure Food and Drug Law, who was also a founder of the Association of Official Agricultural Chemists.

O'Dean L. Kurtz and Kenton L. Harris will share the 1963 award. Mr. Harris is Assistant to the Director, Bureau of Biological and Physical Sciences, Food and Drug Administration. Mr. Kurtz has recently opened a consulting office in Washington, D. C. where he will specialize in analytical sanitation for foods and drugs.

The president of the AOAC, Dr. F. W. Quachenbush, announced the award. He stated the Mr. Kurtz and Mr. Harris had pioneered research and investigations in the field of analytical entomology. They are joint authors of *Micro-Analytical Entomology for Food Sanitation Control,* the authoritative volume on analysis of insect contamination of food and drugs.

Mr. Kurtz and Mr. Harris have both been active in the work of the AOAC and the American Association of Cereal Chemists. They have jointly conducted a number of training courses on micro-analytical sanitation, and in 1958 they both received awards from the Food and Drug Administration for "Special Work Performance."

Report to the Council on Consumer Information—1963

By GEORGE P. LARRICK

Mr. Larrick Is Commissioner of Food and Drugs, United States Department of Health, Education and Welfare. He Presented This Paper at the Annual Conference of the Council on Consumer Information, Washington, D. C., March 22, 1963.

DURING THE PAST YEAR a West Coast family became ill after eating a meal which included a new heat-and-eat frozen food product. They had bought two packages, one of which was eaten and the other stored in the home freezer. Two weeks later the second package was heated and eaten. Again all five members of the family became ill and one had to go to the hospital.

The hospital called the County Health Department. They in turn reported the occurrence to the San Francisco District of the Food and Drug Administration. Since no packages were left of the original purchase, the FDA Inspector collected samples from the local supermarket. Bacteriologists at the San Francisco FDA laboratory checked the samples and found staphylococcus bacteria in quantities sufficient to cause the reported illnesses. A seizure action was immediately filed in the federal court against the remainder of the shipment in the hands of the local distributor and it was thus promptly taken off the market.

Meanwhile, the San Francisco District had reported its findings to the District where the manufacturer was located. Another FDA Inspector visited the factory and found conditions that would have led to the bacterial contamination of the product. Several other lots that had been distributed were seized and the company undertook a nationwide recall of all of the suspected products. A total of $211,000 worth of this food item was destroyed. The company, now very much aware of the need for strict sanitary and bacteriological control of its operations, promptly made very extensive improvements in the plant and

adopted procedural changes costing altogether almost a quarter of a million dollars.

This case history illustrates several important points. It demonstrates, of course, that when foods are prepared on a mass production basis to be served in many thousands of homes it is vitally necessary that safe practices be followed and that there be effective enforcement procedures to ensure this.

Impact of Industrial Technology

But this story makes two other important points about the present problems and responsibilities of the FDA. The first of these is the very great impact of industrial technology, shown in the development of a host of new products which frequently raise new questions and problems of consumer protection. This is characteristic of all the industries we are concerned with—foods, drugs, cosmetics, therapeutic devices and chemical products used around the home. We are continually confronted with the task of keeping up with the new technology of dynamic industries.

Major Responsibility on Manufacturers

The second point of this story is the fact that consumer protection is not really achieved until industry has taken the necessary steps. We commonly say that the *law* protects the consumer, or that the *FDA* protects the consumer, but neither one is effective until the manufacturers comply with the law. In the last analysis, they have to deliver the protection. And the law puts the major responsibility on them.

This leads to another important and fundamental concept.

Preventive Rather Than Punitive Enforcement

The consumer is better protected when steps are taken to *prevent* injury and law violations than by merely punishing violators afterward. This principle underlies a basic trend in the Federal Food, Drug and Cosmetic law over the past 25 years. During this quarter century a series of major amendments have converted the law from a primarily punitive statute into one that contains many built-in procedures for assuring the safety of foods and drugs prior to marketing. Among these provisions are those requiring the certification of insulin and antibiotic drugs, the clearance of new drugs, and the Pesticide, Food Additive and Color Additive Amendments to the Act.

Latest Amendment to Apply Preclearance Principle

The latest amendment to apply the preclearance principle is the provision in the Kefauver-Harris Drug Amendments of 1962 requiring that new drugs be shown to be *effective*, as well as safe, before they are marketed commercially. This law also imposes new safeguards on the investigational use of the new drugs and new antibiotics to prevent injury while the drugs are being studied prior to their commercialization.

The Federal Food, Drug and Cosmetic Act today reflects the complex industrial technology of our times—an ever-increasing technology. It is an effort by our society and our lawmakers to cope with this technology and to ensure that its benefits will to the greatest possible extent outweigh the risks and hazards. The law in fact is based on the same technology which brought it into being. It requires all producers to achieve standards which have already been demonstrated to be workable.

Such a technology and such a law require far more in the way of communication and education than we once thought to be sufficient. The fact is that extensive and continuing communication is essential in securing industry compliance with this law.

Such communication is very much in the interest of consumers. Last month we had 700 people in this room which normally holds about 500, for a conference on the proposed regulations under the new drug amendments. We had 11 people on the platform answering questions, and the questions went on all day.

Need for More Communication with Consumers

I sometimes think that if consumers were to become as interested in the Food and Drug law as industry, then all our problems would be solved—or perhaps just beginning! At any rate, we would be able to do a much better job. Certainly we need more communication with consumers than we have had in the past, and through our Consumer Consultants and our Division of Public Information we are taking some steps to accomplish this.

Here might be a good place to call your attention to our exeprimental museum which you will find on the third floor just opposite the elevators. The theme of this exhibit is:

"Science Working Through Law to Protect Consumers."

Here also we call your attention to our Monthly Report and our Memo for Consumers, which are available to all of you if you wil request in writing to be put on the appropriate mailing lists.

Now I should like to report on recent developments that are o special significance to consumers.

Recent Developments of Special Significance to Consumers

All of us realize that a law like the Federal Food, Drug and Cosmetic Act is neither static nor perfect. New developments frequently require changes in the law to meet new problems and conditions. The amendments I mentioned earlier were designed to meet such problems. But there are other needs which have not been met. For example, there is no requirement in the law that cosmetics be proved safe before marketing, or that new medical devices be cleared for safety and effectiveness. Our inspection authority is limited in ways which seriously handicap our law enforcement efforts. We are barred from seeing certain records which are required in determining whether or not firms are complying with the law, and that are essential to preventive rather than punitive enforcement. Another serious need is for stronger control over sedative and stimulant drugs which are widely diverted into illegal channels. I am speaking particularly of the so-called sleeping pills and pep pills which are involved in crime, highway accidents and delinquency.

Bills dealing with these problems have been pending in Congress for years. President Kennedy summarized the need for such legislation in his message on consumer problems February 14, 1962. The legislation was combined in two so-called "omnibus bills" that were introduced in the last Congress. One of these bills dealt largely with prescription drugs and the other with cosmetics and therapeutic devices. Hearings were in progress.

Then, as you all know, the tragic story of thalidomide hit the headlines. A major medical disaster had occurred in Europe—thousands of armless and legless babies had been born to mothers who had taken this supposedly harmless drug. But it had been kept off the market in the United States by the FDA Bureau of Medicine acting under authority of the New Drug Section of the 1938 law. Dr. Frances Kelsey, who reviewed the application, with the concurrence of her medical associates was not satisfied with the data submitted. She

insisted on answers to her questions and more information. By so doing she delayed action on the application which would otherwise have become effective automatically. Months went by and then came the shocking disclosures in Germany.

The thalidomide experience dramatized for the American public the great importance of adequate controls for drugs. Congress responded by enacting the legislation now known as the Kefauver-Harris Drug Amendments of 1962. This law is a major advance in consumer protection. I would like to summarize it briefly.

Summary of Kefauver-Harris Drug Amendments of 1962

(1) Drugs are defined as adulterated if they are produced in a plant that is not equipped and operated in conformity with good manufacturing practices that will result in all drugs being produced under conditions adequate to ensure their safety, identity, strength, quality and purity.

(2) From now on, before a new drug is approved for marketing, it must be shown that it will have the effect it purports or is represented to have. Heretofore, only clearance for safety was required.

(3) When new information raises questions about the safety or effectiveness of a previously cleared drug the new law provides for the drug to be withdrawn promptly from the market. A new drug may also be required to be withdrawn if the manufacturer fails to maintain the required controls or keep the necessary records, or refuses to give FDA access to such records.

(4) Manufacturers are required to report promptly to FDA any information they get regarding adverse effects from new drugs and antibiotics that are on the market.

(5) Authority is provided for much tighter control over distribution of drugs for research purposes before approval for marketing. Both patients and physicians who take part in clinical investigations will be better protected by these regulations, and they will likewise contribute to higher professional and scientific standards in medical research.

(6) All antibiotic drugs for human use are made subject to testing in the FDA laboratories and new batches of these drugs may not be shipped unless they are certified by the FDA as safe and effective. Exemptions are directed if certification is found to be unnecessary.

(7) Authority to inspect establishments manufacturing prescription drugs is strengthened to encompass access to many things previously immune to inspection.

Consulting laboratories doing work for drug firms on a fee basis are specifically included as establishments subject to inspection.

Federal courts are given jurisdiction to issue injunctions against refusal to permit inspection authorized by the Food, Drug and Cosmetic Act. This applies not only to prescription drugs but to all articles covered by the Act. Previously, the only remedy for refusal to permit inspection was criminal prosecution.

(8) Every drug manufacturing establishment in the United States, regardless of whether it is engaged in interstate or intrastate commerce, must register annually with the Department. We are directed to inspect them at least once every two years.

Manufacturing establishments in foreign countries may register. If they do not, a sample from each of their importations is to be made available to us for analyses.

(9) Authority is provided to designate "established names" for drugs when this is desirable in the interest of usefulness and simplicity.

(10) Advertising of prescription drugs must include (a) the established name in type at least half as large as the brand name; (b) the drug's quantitative formula to the extent required on its label; and (c) a true and non-misleading brief summary of information as to adverse side effects, contraindications, and effectiveness of the drug for the guidance of physicians.

The advertising provision is of special interest because, for the first time, an advertising law has been enacted that is enforceable in the courts by seizure, injunction or criminal prosecution. You may recall that the 1938 Wheeler-Lee Amendment to the Federal Trade Commission Act dealt with advertising to the medical profession in a limited way. Only materially misleading statements could be challenged. In contrast, the Kefauver-Harris Amendments to the Federal Food, Drug and Cosmetic Act require advertising to the medical profession to be not only free from false and misleading claims, but also to include affirmative disclosures concerning side effects, warnings and precautions. Thus Congress has shown its intention to require that advertising matter, as well as labeling, shall provide physicians with

vitally necessary information regarding the drugs they prescribe and administer to their patients.

As you can see, the Kefauver-Harris law is a very important advance in the field of consumer legislation. Likewise, it is a great challenge to the FDA and to the drug industry. We in the FDA are confronted with a most difficult task of administration that requires the enlargement and strengthening of our medical staff to handle the greatly increased and more complex responsibilities. The drug industry is challenged with higher standards in both medical research and drug production. I believe that a good beginning has been made toward the accomplishment of these objectives.

Conclusion

There are many other topics which I could appropriately report on at this meeting but there is not enough time.

We have been delighted that the Council on Consumer Information decided to meet in Washington this year. Your organization is one of great importance today, and potentially even more so in the future. In these times, consumers need to be informed as never before. From many years of observation I can tell you that consumers have a habit of neglecting their interests except at those rare times when they get excited about something. It takes an organization to develop an effective, consistent program for informing the consumer. The government is trying to do its proper share in this. We in the FDA are hopeful that consumers will continue to take an interest in their problems as consumers. We hope you will be inquisitive and communicative. Let us know when you encounter anything that comes under our jurisdiction that you think is detrimental to your interests. This often helps us to help you. [The End]

New Challenges Ahead in Maintaining the Integrity and Quality of Our Food Supply

By K. L. MILSTEAD

This Paper Was Part of a Panel Discussion Presented at the Annual Convention of the National Canners Association on January 20, 1963, in Chicago, Illinois. The Author Is Deputy Director of the Bureau of Enforcement, Food and Drug Administration.

THE SUBJECT of this panel discussion presupposes, it seems to us, two facts:

(1) Our food supply today is safe and of high quality but,

(2) There are real or imaginary challenges to this situation which we can identify and which must be met if the integrity of our food supply is to be maintained.

On the first point, we in the Food and Drug Administration support the position that the consumers in this country enjoy the safest, cleanest, most nutritious and most attractive food that any people have ever known. This is not to say that there is no unfit or low quality food on the market, for the daily record of regulatory actions clearly shows that this is not the case. But, taking into consideration the magnitude and complexity of the problem of producing, processing, packaging and distributing the quantity and variety of food required to feed nearly 190 million people, the combined efforts of regulatory officials and the industry to safeguard the food supply has kept the amount of unfit food reaching consumers unquestionably small.

We also support the position of the other panelists that the charges of the alarmists, food faddists, health food promoters and do-gooders that our food supply is poisoned, that its nutritive qualities have been destroyed or impaired and that commercially produced foods are the cause of most of the ills of mankind are without foundation.

Having agreed that our today's food is safe and of good quality, what then are the challenges ahead that question whether this will continue to be the case. While there are several problems that we could discuss, such as nutritional quackery, microbiological contamination of foods, sanitation, radioactive contamination, the use of health claims in the promotion of foods, and so forth, I want to confine my brief remarks to what we believe is the most urgent problem.

Safe Use of Chemicals Is Challenge of the 60's

The paramount challenge of the 60's as we see it is to insure the *safe* use of a multitude of chemicals permitted in the production, processing and distribution of our nation's food supply: pesticides—food additives—color additives. Grave questions by thoughtful people are being raised about the capacity of our agriculture, the food industry and the government to assure consumers that the chemical tools which have brought our food technology to such a high point of efficiency present no hazard to the public health. As the government agency charged with the responsibility of maintaining the safety of our food, we must be able to answer these questions with facts that are unassailable. Agriculture and the food industry must also be able to answer these questions with irrefutable facts based on accurate knowledge and not by unsupported statements based on emotion and conjecture.

This challenge will continue to be more pressing as our population grows and our technology develops. We agree that we cannot continue to produce adequate amounts of food at reasonable prices and protect it from deterioration without chemicals. As was pointed out in a recent editorial in a national magazine, the problem is not whether the wise use of chemicals is necessary, but rather whether the utmost intelligence is being exercised in their use and adequate controls and facilities are available to prevent their misuse.

Need for Supervision

Congress has charged us with the responsibility of not only deciding whether chemicals can be used safely at all, but of supervising their use within tolerance limitations and of taking necessary enforcement action when they are misused. We propose to discharge this responsibility and to meet this challenge by the most vigorous and expanding enforcement, educational and scientific research programs that our resources and facilities will permit. This includes

not only the careful scrutiny of all scientific data submitted to us before any new pesticide, food additive or color additive is permitted, but an enlarged inspection and surveillance program to see that the conditions on which these uses were permitted are actually being observed in practice. We will cooperate fully with all state agencies and assist and encourage them in every way in their enforcement and control activities.

Our purpose—indeed the high purpose of the new laws which we are administering—is to prevent misuse of additives. The design of these laws is to apply advance approvals and controls to restrict additives within safe limits. When the law is working effectively, enforcement is needed only in those unusual circumstances where directions have not been followed or where an occasional misadventure occurs. In fact, the need for a large-scale enforcement operation would throw into question the scientific validity of the approval and would call for its prompt re-evaluation.

Cooperative Program Needed

We want to work closely with your association and your members to develop a cooperative program to meet this challenge. We invite your association to confer with us and let us know what information or other assistance we can furnish you. We urge you to bring to our attention promptly any information you acquire that indicates that any food contains more of an additive than permitted so that all possible steps can be taken to deal with it before it becomes a threat to consumers and an unanswerable question of national concern.

This is *our* problem, and it demands *our* complete cooperation in the interest of consumers. We must develop a broad federal-state-industry-consumer-cooperative program that will not only insure the safe use of chemicals in our food but will do so in such a way that complete confidence in food additives, in pesticides, in color additives and in the industry and government agencies who follow this use can be maintained.

It is our view that this can be accomplished only through an adequate preventive and educational program that will keep the necessity for enforcement actions at a minimum. Every legal action involving unsafe chemicals in our food represents a failure on the part of us all to exercise the intelligence and wisdom to prevent misuse. Every legal action where safety is involved raises a question that cannot be adequately answered to consumers. Every legal action

makes the answers to the questions of the alarmist and faddist more difficult. There is no acceptable explanation for poisonous food. The consumer has the right to expect that his food will be beyond reproach.

Prompt Law Enforcement Necessary

We are not suggesting that there is an alternative to prompt and vigorous legal actions when we find foods that are contaminated. Any failure to act would also lead to lack of confidence in the food supply. As Commissioner Larrick stated recently at the joint meeting with the Food Law Institute [1]:

> There is one thing we must not overlook—the Food and Drug Administration is a law enforcement agency. . . . And we will continue to give the American public honest, vigorous enforcement of the statutes we administer. This means that there will be court actions where there are violations of the law.

What we are suggesting is that your industry and the regulatory agencies can meet this challenge through a program of cooperation, self-regulation and due care that should and must attend the use of toxic substances in food technology.

We are also suggesting that the only real challenge that exists to the safety and quality of our food supply is the challenge to our thinking and to our ability to work together to contain and control our expanding technology.

Conclusion

We cannot meet this challenge with procedures and controls of the past. We must agree quickly on an adequate inspection-surveillance program by both industry and government. There must be no withholding of information nor dealing at arm's length by either side if we are to accomplish our objectives.

Our attention must be directed to meeting the real and urgent problems created by the products of modern science and technology. We have no time to waste arguing about little matters among ourselves when we are being challenged from many sides to answer the question "Is Our Food Safe?"

What differences exist now or may develop between us, let's reconcile them promptly so that we can meet this challenge with strength and move forward with the confidence expressed by the Psalmist:

"Therefore will we not fear, though the earth do change."

[The End]

---

[1] 18 FOOD DRUG COSMETIC LAW JOURNAL 13, 18

FOOD DRUG COSMETIC
LAW JOURNAL

PUBLISHED BY
COMMERCE CLEARING HOUSE, INC.,
PUBLISHERS of TOPICAL LAW REPORTS
4025 W. PETERSON AVE., CHICAGO 46, ILL.
RETURN REQUESTED

SECOND CLASS POSTAGE
PAID AT CHICAGO, ILLINOIS

A COMMERCE CLEARING HOUSE PUBLICATION