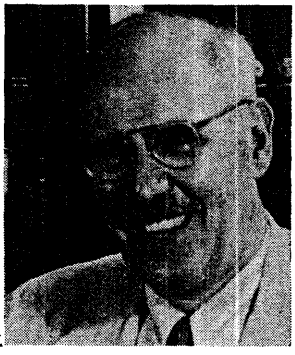
A Half-Century of Drug Control

By JAMES C. MUNCH

Fewer Than 10 Per Cent of Present Prescriptions Could Have Been Filled in 1906, Says the Writer; Ingredients Were Unknown or Unavailable. He Expects Similiar Progress with Continued Research

THE DEVELOPMENT of drug therapy during recorded history reveals changes from the empiric toward the scientific and from the processes of trial and error (trials leading to survival and errors to death) to our present scientific knowledge based on chemical constitution and pharmacological action permitting (1) predictions of effects to be expected and (2) preparation of new synthetic compounds of known structure with predicted therapeutic activity. This process of evolution is still expanding. It seemed interesting to determine the status of drugs and their preparations in 1906, and the significant steps during a half-century in developing control over them at the federal level. It has not been possible to include equally important developments at the state and municipal levels, or control under the postal laws, Federal Trade Commission Act, Federal Caustic Poison Act, Federal Insecticide, Fungicide, and Rodenticide Act, or other pertinent laws. Control over morphine, cocaine and other narcotic drugs was transferred to the Federal Bureau of Narcotics by the Harrison Act of 1914, control of whiskey and other alcoholic beverages to another branch of the United States Treasury. Even though many of the decisions of the courts upon cases involving foods or cosmetics are also applicable to drugs, they have also been omitted in this consideration.

An act was approved by President Harrison on August 30, 1890 (26 Stat. 415), prohibiting the importation of adulterated drugs, food



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or liquor, under penalty of forfeiture and fines up to $1,000, or one year's imprisonment. This amplified the earlier act signed by President Polk on June 26, 1848 (9 Stat. 237), passed to prevent the importation of adulterated and spurious drugs and medicines which failed to meet the standards of the United States, Edinburgh, London, French or German pharmacopoeias; these were prohibited entry and were to be re-exported or destroyed.

The early studies in the Division of Chemistry of the United States Department of Agriculture dealt largely with foods, although some attention was given to analytical methods. When Dr. Harvey W. Wiley joined the group in 1883, additional efforts were expended and there was an increasing public interest in foods. This was climaxed by the appearance of Upton Sinclair's *The Jungle* in 1905. Attention to existing misrepresentations and claims for drugs and drug preparations were so exaggerated as to lead to disrespect for the terms "patent" and "proprietary" remedies, even though many of the manufacturers at that time endeavored to tell the truth and to make proper claims for their products. The series of articles by Edward W. Bok during 1904 and 1905 in the *Ladies' Home Journal* and by Samuel Hopkins Adams in *Collier's* under the title "The Great American Fraud" revealed many of these excessive claims. These publications appear to be the trigger mechanisms stimulating popular and Congressional interest in the passage of suitable control legislation. Since the original proposal of Hendrick B. Wright of Pennsylvania on January 20, 1879, for a federal control act, some 190 bills had been proposed, and hearings led to increasing interest in drugs as well as foods. Support for legislation was forthcoming from producers, importers and drug

manufacturers, as well as consumers. This finally led President Roosevelt to say in his message to Congress on December 5, 1905:

> I recommend that a law be enacted to regulate interstate commerce in misbranded and adulterated foods, drinks and drugs. Such law would protect legitimate manufacture and commerce, and would tend to secure the health and welfare of the consuming public. Traffic in foodstuffs which have been debased or adulterated so as to injure health or to deceive purchasers should be forbidden.

As a result of hearings before the House and the Senate, an Act was drafted by Dr. Wiley with his associates; proposed by Senator Weldon B. Heyburn of Idaho; passed by both houses of Congress; and signed by President Theodore Roosevelt on June 30, 1906 (21 USCA 1, 34 Stat. 768). This Federal Food and Drugs Act of 1906 (referred to as the 1906 Act hereafter) contained definitions and requirements: "For preventing the manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein."

Provisions of 1906 Act

Section 1 prohibited *manufacture* of any adulterated or misbranded drug as a misdemeanor, carrying a fine not to exceed $500 or one year's imprisonment, or both, upon conviction. Each subsequent conviction carried a fine of not less than $1,000 or one year's imprisonment, or both.

Section 2 prohibited *introduction* into any state or territory or the District of Columbia from any other state, territory or the District of Columbia, or from any foreign country, or *shipping* or *receiving and delivering* in original unbroken packages adulterated or misbranded drugs as a misdemeanor with fine not exceeding $200 for the first offense, and not exceeding $300, or imprisonment not exceeding one year, or both for each subsequent offense. Drugs were not misbranded or adulterated when exported in accordance with directions of a foreign purchaser.

Section 3 authorized the Secretaries of the Treasury, Agriculture, and Commerce and Labor to make *rules and regulations* for carrying out provisions of this Act.

Section 4 directed that *examinations* of drugs should be made in the Bureau of Chemistry of the Department of Agriculture to determine whether they were adulterated or misbranded. If so, the party from whom the sample was obtained should be given a *hearing*.

If it appeared that any of the provisions of this Act had been violated, the Secretary of Agriculture certified the facts to the proper United States District Attorney, who was directed (Section 5) to cause proper prosecution. After judgment of the court, notice should be given by *publication.*

Section 6 provided: That the term "drug," as used in this Act, shall include all medicines and preparations recognized in the United States Pharmacopoeia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease of either man or other animals . . . .

Section 7 defined *drug adulteration* under two classes: (1) if it differed from the standard of strength, quality or purity, when sold under a name recognized in the *United States Pharmacopoeia* or the *National Formulary* by tests official at the time of investigation, unless its differing standard was stated on the bottle, box or container; (2) if its strength or purity fell below the professed standard of quality under which it was sold.

Section 8 defined *drug misbranding* as any statement, design or device on the package or label which was false or misleading in any particular (including place of manufacture or production), also for two additional reasons—(1) if it was an imitation, or offered for sale under the name, of another drug and (2) if the original contents had been replaced in whole or in part, or if the label failed to bear a statement of the quantity or proportion of "any alcohol, morphine, opium, cocaine, heroin, alpha or beta eucaine, chloroform, cannibus indica, chloral hydrate, or acetanilide, or any derivative or preparation of any such substances contained therein." (The Sherley Amendment of 1912 added another cause: "If the label or package carries any statement, design or device regarding the curative or therapeutic effect of the article or any of its ingredients which is false and fraudulent.")

Section 9 provided that no dealer should be prosecuted if he had a *guaranty* from the vendor that the products bought were not adulterated or misbranded.

Section 10 provided that an adulterated or misbranded drug being transported or remaining unloaded, unsold or in the original unbroken packages after transfer, or imported from, or intended for export to, a foreign country might be *seized* for condemnation in any district court where found. Such seized article might be sold, destroyed, or released on bond to the owner.

Section 11 provided that the Secretary of the Treasury should furnish samples of drugs offered for *import* to the Secretary of Agriculture for examination. If such drug was adulterated or misbranded, was otherwise dangerous to health, was forbidden entry or sale in the foreign country or was falsely labeled in any respect, admission should be refused and the article exported within three months or destroyed.

Section 12 *defined* "territory" and "person," and placed responsibility for acts of employees on their employers.

Section 13 provided that the Act become *effective* on January 1, 1907.

Only one amendment to the drug provisions of the 1906 Act was made, namely, the Sherley Amendment, prohibiting false and fraudulent statements of curative or therapeutic effect, which followed the decision of the Supreme Court of the United States which became necessary in *U. S. v. Johnson,* 221 U. S. 488, 31 S. Ct. 627. The Gould Amendment or net-weight amendment of March 3, 1913, applied to both drugs and foods. Only foods were involved in the Kenyon Amendment of 1919 regarding wrapped meats, the 1923 act defining butter, the 1930 McNary-Mapes Amendment regarding standards for canned foods and the 1934 Sea Food Inspection Act.

In addition to the testimony given before the various Congressional hearings leading to the 1906 Act and to the Sherley Amendment, which indicated the condition of the drug market at that time, cumulative statistics on drug control may be obtained from the annual reports. Dr. Harvey W. Wiley was the Chief for the fiscal years 1907-1911; R. E. Doolittle, acting Chief for 1912; Dr. Carl L. Alsberg, for 1913-1921; W. G. Campbell, acting Chief for 1922-1923; Dr. C. A. Browne, for 1924-1927, the time of the last report for the Bureau of Chemistry. Reorganizing enforcing agencies, W. G. Campbell, Director of Regulatory Work, signed the 1928 and 1929 reports from the Food, Drug, and Insecticide Administration and then, as Chief of the Food and Drug Administration, those from 1930 through 1938. He continued as Chief under the new Federal Food, Drug, and Cosmetic Act of 1938, for 1939 and 1940, and then as Commissioner through 1943. Dr. Paul B. Dunbar was Commissioner for 1944-1950; C. W. Crawford, for 1951-1954; and Dr. George P. Larrick is the present Commissioner. These annual reports reflect progress during each fiscal year, summarizing previous developments and often suggesting future projects. It should be appreciated that much of the educational and preventive work in drug control is reflected in the decrease in the number of legal actions

undertaken, following cooperative efforts of industry with the Administration.

Statistical information in these reports from 1907 through 1939 reveals development of control under the 1906 Act. For the ten years 1930 through 1939, there were 12,016 drug imports detained, of a total of 49,402 offered, or 24 per cent. This may be compared with the data for the four years 1909-1912 (representing drug imports about the time of passage of the 1906 Act, reflecting control under the earlier laws), during which there were 1,350 rejections of a total of 1,931 drug imports offered, or approximately 70 per cent. In the early years, enforcement was largely by prosecution under Section 2; it was necessary to establish rules and regulations for enforcement, and to obtain judicial interpretations of many sections of the Act. Reports show that during the five years 1908-1912, there were 841 prosecutions dealing with drugs, drug products, preparations and medicines, or approximately 25 per cent of the total 3,350 prosecutions. Similar figures for seizure actions under Section 10 were not included in these reports. However, greater use was made of the seizure provision as enforcement continued. During the last ten-year interval of the 1906 Act, from 1930 through 1939, there were 3,201 prosecutions representing drug control, or 36 per cent of the total 8,804 prosecutions; similarly, there were 3,620 seizures, or 23 per cent of the total 15,666 seizures made. In establishing the project system in 1933, one quarter of the time of the field staff was allocated to drug control projects; percentages for the next seven years ranged from 25 per cent to 33 per cent, averaging 29 per cent.

Studies of the notices of judgment (N. J.'s) published in accordance with Section 4 give another vista of activity in drug control. There was a grand total of 31,157 N. J.'s published under the 1906 Act. Actions against *drugs* (crude drugs and simple preparations in the *United States Pharmacopoeia* and the *National Formulary*) were reported in 2,608 N. J.'s. There were 36 court contests, in which verdicts of guilty were returned in 17 notices and not guilty in 19 notices. Actions against *drug products and preparations* (these include unofficial preparations, patent and proprietary medicines) were recorded in 6,510 N. J.'s. There were 107 court contests involving prosecutions or seizure; verdicts in favor of the government were returned in 68 notices and not-guilty decisions in 39 notices. Combining these actions under *drug control,* there were 143 contests in the 9,118 N. J.'s; for every 1,000 N. J.'s thus combined, there were 16 contests, of which the government won ten. Curiously, these 9,118 comprise 29 per cent of

the total 31,157 N. J.'s issued—almost exactly the percentage of time spent in enforcing the drug phases.

The importance of notices of judgment was stressed by Dr. Alsberg in his 1920 report:

> Indeed, these notices give the most reliable history of the development of the courts' interpretation of the law as well as of the department's policies with reference thereto. Unfortunately, these notices are not sufficiently studied by manufacturers. If they were, infractions of the law could and no doubt, would be avoided by them.

Summary of Actions Prior to 1938 Act

My detailed study of the published N. J.'s in a different connection has indicated certain outstanding cases as indications of the conditions encountered in the drug field, and decisions which helped in the development of drug control under the 1906 Act. Some of the most interesting are reviewed briefly:

(1) N. J. 10 is the first dealing with a drug. Action was brought in the District of Columbia Police Court for selling cocaine hydrochloride without declaring the quantity of drug present. The defendant pleaded guilty. A fine of $100 was imposed.

(2) N. J. 25 was a proceeding against Harper's Cuforhedake Brane Fude, a headache remedy which contained 1 per cent of antipyrine and 15 grains of acetanilide per fluid ounce. The label claimed that the product produced harmless relief without subsequent depression, and that it did not contain any poisonous ingredients of any kind. This was the first contested drug case. In the jury trial before the District of Columbia Police Court, much evidence was presented. The defendant pleaded not guilty; the jury returned a verdict of not guilty, and the court imposed fines of $700, or imprisonment in jail for 150 days. A proposed appeal to the court of appeals was withdrawn, and the fine was paid. In his charge to the jury, the judge pointed out that this law was passed to protect ordinary citizens, not scientific men who know the meaning and value of drugs. An observer was present throughout the trial to notify the druggists of the country regarding details of the case and the decision of the court.

(3) N. J.'s 266, 1,058: *U. S. v. Johnson* became a famous case, leading to the only drug amendment to the 1906 Act. It resulted from a criminal prosecution under Section 2 of Dr. O. A. Johnson, of Kansas City, Missouri, for the interstate shipment of Dr. Johnson's Mild Combination Treatment for Cancer (Cancerine Tablets, No. 1, No. 17, Antiseptic Tablets, Blood Purifier, Special No. 4). Misbranding was

charged because of false claims of effectiveness in the treatment of the cancer, for which these products were worthless. The judge found for the defendant in quashing the indictment; discussing Section 8, it was the court's opinion:

"The package or label of which shall bear any statement, design, or device regarding such article, or the ingredients or substances contained therein which shall be false or misleading in any particular," must be read and interpreted so as to have regard to its context . . . . Having regard to the intendment of the whole act, which is to protect the public health against adulterated, poisonous, and deleterious foods, drugs, etc., the labeling or branding of the bottle or container as to the quantity or composition of "the ingredients or substances contained therein which shall be false or misleading," by no possible construction can be extended to an inquiry as to whether or not the prescription be efficacious or worthless to effect the remedy claimed for it . . . . In the debates in Congress, when this measure was under consideration, it was never sought to be justified except on the ground of protecting the public health, as it might be affected by interstate shipments of foods, drugs, etc. At no time was it asserted or pretended that it was proposed to reach the matter of holding the manufacturers and vendors of prescriptive or patented medicines, multitudinous and multiform as they are, to criminal liability for misstatements as to the curative or remedial effects of the prescription, which would necessarily depend upon the opinions of contending experts and the users of the nostrums. . . . The motion to quash is sustained.

The United States Supreme Court affirmed this decision in their majority opinion delivered by Mr. Justice Holmes:

It seems to us that the words used convey to an ear trained to the usages of English speech a different aim; and although the meaning of a sentence is to be felt rather than to be proved, generally, and here, the impression may be strengthened by argument . . . .

. . . we are of opinion that the phrase is aimed not at all possible false statements, but only at such as determine the identity of the article, possibly including its strength, quality, and purity, dealt with in § 7 . . . .

We shall say nothing as to the limits of constitutional power, and but a word as to what Congress was likely to attempt. It was much more likely to regulate commerce in food and drugs with reference to plain matter of fact, so that food and drugs should be what they professed to be when the kind was stated, than to distort the uses of its constitutional power to establishing criteria in regions where opinions are far apart. See *American School v. McAnnulty*, 187 U. S. 94 . . . .

In dissenting, Justices Hughes, Harlan and Day stated:

In each case the indictment alleged that the article was "wholly worthless," as the defendant well knew. . . .

Articles, then, intended to be used for curative purposes, such as those described in the indictment, are within the statute . . . misbranding is committed if the package or label of such an article bears any statement regarding it "which shall be false or misleading in any particular." But it is said that these words refer only to false statements which fix the identity of the article. According to the construction placed upon the statute by the court below in quashing the indictment, if one puts upon the market, in interstate commerce, tablets of inert matter or a liquid wholly worthless for any curative purpose, as he well knows, with the label "Cancer Cure" or "Remedy for Epilepsy," he is not guilty

of an offense, for in the sense attributed by that construction to the words of the statute he has not made a statement regarding the article which is false or misleading in any particular.

. . . Reading the act with the sole purpose of giving effect to the intent of Congress, I cannot escape the conclusion that it was designed to cover false and misleading statements of fact on the packages or labels of articles intended for curative purposes, although the statements relate to curative properties. . . .

The argument is that the curative properties of articles purveyed as medicinal preparations are matters of opinion, and the contrariety of views among medical practitioners, and the conflict between the schools of medicine, are impressively described. But, granting the wide dominion of opinion, and allowing the broadest range to the conflicting medical views, there still remains a field in which statements as to curative properties are downright falsehoods and in no sense expressions of judgment. This field I believe this statute covers. . . .

I entirely agree that in any case brought under the act for misbranding,—by a false or misleading statement as to curative properties of an article,—it would be the duty of the court to direct an acquittal when it appeared that the statement concerned a matter of opinion. Conviction would stand only where it had been shown that, apart from any question of opinion, the so-called remedy was absolutely worthless, and hence the label demonstrably false; but in such case it seems to me to be fully authorized by the statute.

Based upon this decision, a number of other actions by the Bureau of Chemistry alleging false and misleading therapeutic claims were dismissed by various courts. This situation led to a special message to the Congress by President Taft:

In my opinion the sale of dangerously adulterated drugs, or the sale of drugs under knowingly false claims as to their effects in diseases, constitutes such an evil and warrants me in calling the matter to the attention of the Congress. Fraudulent misrepresentations of the curative value of nostrums not only operate to defraud purchasers, but are a distinct menace to public health. There are none so credulous as suffers from disease. The need is urgent for legislation which will prevent the raising of false hopes of speedy cures of serious ailments by misstatements of fact as to worthless mixtures on which the sick will rely while their diseases progress unchecked.

This was remedied by the passage of the Sherley Amendment, signed by President Taft August 23, 1912, adding the third subdivision to Section 8.

(4) N. J. 4816 records the decision of the United States Supreme Court in affirming judgment in the District Court for Nebraska in *Seven Cases of Eckman's Alternative v. U. S.*, 239 U. S. 510. Delivered by Mr. Justice Hughes, it reaffirmed his position in *U. S. v. Johnson.* He stated that the principal question in this case was the validity of the Sherley Amendment. Dismissing the objection that it entered the domain of speculation and uncertainty, he stated:

Congress deliberately excluded the field where there are honest differences of opinion between schools and practitioners . . . . It was, plainly, to leave no

doubt upon this point that the words "false *and fraudulent*" were used. . . . the statement contained in the package was put there to accompany the goods with actual intent to deceive. . . . persons who make or deal in substances or compositions alleged to be curative are in a position to have superior knowledge, and may be held to good faith in their statements. . . . Congress recognized that there was a wide field in which assertions as to curative effect are in no sense honest expressions of opinion, but constitute absolute falsehoods, and in the nature of the case can be deemed to have been made only with fraudulent purpose. The amendment of 1912 applies to this field and we have no doubt of its validity.

In this decision it was ruled that the word "contain" in the amendment covered circulars or printed matter placed inside the package. The power of Congress does not depend on the question of whether the statement is *on* or *in* the package which is transported in interstate commerce.

(5) N. J.'s 1056, 3868 trace actions against labeling in *U. S. v. Antikamnia.* Seizure was made in the District of Columbia on the ground that the label declared that the product did not contain acetanilide; the presence of acetphenetidin was declared but not definitely stated to be a derivative of acetanilide. The district court sustained exception to this libel on the basis that Regulation 28 by the Secretary went beyond the bonds of the law in requiring such a declaration. The Supreme Court affirmed this decision, denying the charge of the government that:

. . . each and all of them [said labels] bear the statement that no acetanilid is contained therein, and that the statement imports and signifies that there is no quantity of any derivative of acentanilid contained in the drug.

It must be determined whether a derivative acts in the same manner as the original chemical. The United States Supreme Court (231 U. S. 654) reversed these decisions, holding that a derivative is so related to a substance that it would be regarded as obtained from the latter by actual or theoretical substitution, whether it is actually produced therefrom or not:

The composition of drugs is a matter of technical skill, their denomination often by words of scholastic origin, conveying no meaning to the uninformed, their uses and abuses learned only by experience, beneficial or evil. . . . Experience had demonstrated the quality of those substances, their effects had become common knowledge; their names, therefore, were all the warning it was necessary for the law to give. But derivative of them might, probably would, be of their quality, so derivatives of them were to be guarded against, and the law hence further provided that the labels on them should state the "quantity or proportion" of "any derivative or preparation" of them. . . .

The purpose is to prevent the surreptitious sale of certain noxious drugs or their derivatives, the latter supposedly partaking of the quality of parent article and as effective of evil consequences. . . . No serious burden is thereby imposed on honest business. Indeed, it makes the label on the packages an assurance

as well as a warning, and benefits all concerned, manufacturer, seller, and purchaser. And this in the interest of the public health.

(6) N. J.'s 3869, 4310: Seizure was brought in the District of Columbia against Buffalo Lithia Water as being misbranded, since it did not contain an appreciable amount of lithium, and therefore would not give the therapeutic effect of lithium. The product was recommended in all affections due to uric acid diathesis, gout, rheumatism, and stone in the bladder, kidneys or liver. Chemical analysis showed no appreciable amount of lithium in the size of bottle usually sold; spectroscopic analysis showed 0.002 mg/liter, or one grain in 10,000 gallons of water; the average dose of lithium as a uric acid solvent was from 5 to 7.5 grains three times daily:

> So that, for a person to obtain a therapeutic dose of lithium by drinking Buffalo Lithia Water he would have to drink from 150,000 to 225,000 gallons of water per day . . . Potomac River water contains five times as much lithium per gallon as the water in controversy.

The claimant stressed the point that this was natural mineral water collected from a spring known as the "Buffalo Lithia Spring." The court concluded that if no natural water contained sufficient lithium to give a therapeutic effect by drinking a reasonable quantity, it would prove that the other so-called lithia waters were also misbranded.

(7) N. J. 4849: *U. S. v. Dr. Williams' Pink Pills for Pale People,* 233 F. 71, was a jury trial of a seizure, with verdict for the government, which was affirmed by the Circuit Court of Appeals for the Third Circuit. Claims were made on the label that the product was:

> . . . [a] safe and effective tonic for the blood and nerves for anaemia, diseases due to impoverished blood, such as rheumatism, diseases of women, nervous disorders resulting from malnutrition including neuralgia, sciatica, St. Vitus' Dance, useful in local locomotor ataxia and partial paralysis. A digestive tonic for dyspepsia and chronic constipation.

The enclosed circular extended the scope of these diseases. Giving language its ordinary and common meaning to an ordinarily intelligent person who would purchase these pills, the judge charged the jury to determine from the evidence whether those statements were false. The object of the Act is to prevent credulous and ignorant people and the public generally from being deceived in the purchase of proprietary medicines such as these. In determining whether these statements were fraudulent, the jury should determine whether the claimant knew they were false in making them, with intent to defraud:

> . . . or with such wilful and gross negligence to inquire into the effects of these medicines before making the statements, that the intent would be presumed . . . . As I read the labels, there is no direct statement that these pills are cures

for the various sorts of disease mentioned. The general effect of the statements is that the pills are valuable as a tonic for the blood and nerves, and that they are valuable for use in cases where the ailment is the result of or is accompanied by anemia.

The circuit court ruled that the case had been tried properly. Referring to claims of value for treatment of locomotor ataxia, the court ruled that witnesses had testified that the pill would not and could not have any beneficial effects and that the witnesses were experts in medicine and, therefore, giving the consensus of medical opinion.

(8) N. J.'s 7657, 8360: The decision of the district judge in Texas favoring seizure of A Texas Wonder was upheld by the Circuit Court of Appeals for the Fifth Circuit. This product was recommended for kidney and bladder troubles, gravel, diabetes, weak and lame backs and rheumatism; misbranding was charged in that it contained no ingredient or combination of ingredients capable of producing curative or therapeutic effects claimed. The defendant claimed the product contained sweet spirits of niter and oil of juniper instead of turpentine reported by the government. The government presented evidence by physicians of the medicinal properties of this product, from which the court concluded that every claim on the label was false; it had more concern regarding the fraudulent nature. Persons who make or deal in medicines should have superior knowledge of their actions:

> But the slightest reflection upon the well-known fact that persons given to self-medication are credulous and partisan, and prone to deny nature credit for their recovery, and that on this well-known trait of human nature these compounders of specifics and nostrums build their business, deprives this claim of any weighty significance; because it will not do for a person who has been able to prey upon the credulity of a community to escape the consequences of his acts by the very success of his schemes . . . . The danger and injury to the public from this character of advertisement is, however, considerable, in that it induces persons to rely in serious cases, upon a preparation without healing virtue when [but] for this reliance, they would no doubt secure proper advice and treatment for the ills which affect them.

The court sustained the seizure, and decision was affirmed on appeal. This was followed by a very large number of seizures to remove the material from the market. In this connection, the testimony of the defendant should be noted: He had not attended any medical school; he had traveled around the countryside with various doctors; while he had been sick, he had experimented on himself to develop this formula; he had received a large number of glowing testimonials from laymen; he felt that he was not guilty of fraud in

using them; however, he had no reports of critical medical investigations of his product. This same issue of the value of testimonials from laymen to support a medicinal preparation, in contrast to testimony by physicians that it was worthless or definitely harmful, appears in a number of cases. Courts emphasized that the fact that a product did not produce injury or harm did not justify its sale, since it would lead the purchaser to defer consultation or inquiry which might help if taken in time.

(9) N. J. 18,653: The seizure in *U. S. v. Lee's Save the Baby* was tried on the basis that the product falsely and fraudulently claimed curative and therapeutic effects in the treatment of croup, coughs and sore throat, whereas it contained no ingredients effective in these diseases. Analysis showed the presence of camphor, rosemary and origanum oils, Canada balsam and alcohol in lard. The defense presented experienced physicians who testified that these ingredients were valuable in the treatment of these conditions, and that they had used them successfully in their practices over a number of years. The libel was dismissed by the court. This demonstrates the value of clinical evidence to support therapeutic claims for drug preparations.

(10) N. J.'s 671, 19,651: Apparently the first action against B. & M. External Remedy was seizure in New Hampshire, with jury trial in the federal district court on December 19, 1922, on a charge of misbranding under the Sherley Amendment. Analysis showed it to be an emulsion of turpentine, ammonia, formaldehyde and salicylic acid. It was labeled as a remedy for tuberculosis, pneumonia, asthma, coughs, colds, rheumatism, neuritis, peritonitis, locomotor ataxia, blood poisoning, sprains and burns and as an antiseptic. The claimant had no medical training whatever, but had been a court stenographer for a number of years before purchasing this formula in 1913 and starting in business. It had been used on beasts and men previously; he offered testimonials of laymen to support his statements. The government placed a number of physicians on the stand who testified that the product would not be efficacious. The defense claimed that this was a mere difference of opinion between different schools of medicine and that any person setting forth his opinions which disagree with those of the experts may do so, but he must have an honest belief that he is right. The judge further cautioned acceptance of testimonials, since the authors may have been deceived regarding the nature of their disease or the effect of the drug thereon, or they may have been on

the road to recovery before the remedy was used; they cannot testify to the effect of the remedy on the disease, but only on their symptoms. The jury returned a verdict in favor of the claimant. This led to a series of investigations and trials of the product by two sanitariums which found it worthless and, after ten years, a further seizure was made. This led to an extensive and expensive trial in Baltimore, which resulted in victory for the government. The difficulty here was that of establishing fraudulent intent.

In 1903, Dr. Wiley established the "poison squad" of 12 adult men in the Bureau, to determine the physiological effect of ingesting various food preservatives (sulfites, benzoates, salicylates, borates, nitrates, formaldehyde), and copper and aluminum salts, also saccharin as an artificial sweetener. Studies on the composition of drugs on the American market were under way in cooperation with the Council on Pharmacy and Chemistry of the American Medical Association, to confirm and extend reports on nostrums and quackery. Toxicity studies were started on coal-tar colors, and a permitted list was drafted. In 1908, a pharmacology laboratory was established.

Attention was directed to the quality of domestic and import samples of crude drugs, particularly digitalis, ergot, belladonna, henbane, colocynth and asafoetida. "Oil of wintergreen" was consistently adulterated with synthetic methyl salicylate. A number of remedies for consumption and asthma did not contain any drug having remedial value. A number of "cancer cures" were found to contain arsenic or escharotic zinc chloride. An attempt was made to determine the consensus of medical opinion regarding harmful effects from misuse of acetanilide, antipyrine and acetphenetidin in headache remedies; promiscuous usage had been reported to produce poisoning, habit formation or addiction, and death. A number of "soft drinks" contained cocaine—from traces to large proportions. Mail-order "drug addiction cures" recommended for the treatment of addicts were supplying solutions containing decreasing proportions of morphine, unlabeled. A number of soothing syrups were found to be dangerous to infants because of the presence of opium or its alkaloids. Laboratory studies were started upon a number of anthelmintics, including oil of chenopodium. About this time, charges were brought against Dr. Wiley for improper conduct, including the retaining of Dr. H. H. Rusby as an expert in the field of pharmacognosy at a rate greater than the conventional per diem. Congressional investigation of these and other

charges led to his complete exoneration, after which he retired from the Bureau of Chemistry in the spring of 1912.

Investigations were continued on hydrogen peroxide, ginger, headache remedies, essential oils, caffeine and opium and on alleged cures for cancer, consumption, drug addiction, epilepsy, rheumatism and kidney and liver complaints. Special attention was required for medicines supplied by manufacturers directly to physicians, as well as to the quality of many prescriptions furnished by apothecaries. A pharmacognosy laboratory was established. With the passage of the Sherley Amendment, attention was directed to mineral waters with exaggerated claims; to simple household remedies; and to veterinary medicines, including worthless products for hog cholera. Attention was directed to therapeutic claims on labels and circulars, and a distinction was made between drug products intended for over-the-counter sale and those intended for distribution on prescription only. Seizure campaigns were conducted for several years against products for the "cure" of venereal diseases, leading to the elimination of these products from over-the-counter sale. These campaigns were broadened to cover proposed treatments for "lost manhood" and for "suppressed menstruation" (some of which frankly carried abortifacient claims).

In 1922, the office of drug administration was formed to handle proceedings under the Sherley Amendment. Many domestic crude drugs were detained because of the presence of more than 20 per cent of dirt, leading to a cooperative educational campaign to improve methods of cultivation, collection, drying, packaging and storing crude drugs. Campaigns were started to remove unfit anesthetic chloroform, nitrous oxide, ethylene and ether from the market. The extreme variations observed in the chemical analysis of 700 lots of tablets for the purpose of determining proper tolerances led to a series of conferences with the drug industry, from which emerged a "contact committee." This was formed jointly by the control chemists from the drug industry and the government to study methods of assay and to establish tolerances for drug preparation. At this time, bioassays were developed to supplement chemical methods and reference standards prepared for distribution to laboratories throughout the world. Seizure actions were taken against a number of products represented as valuable in the treatment of appendicitis, cancer, coughs, colds, diabetes, gall stones and tuberculosis.

Investigations were started against antiseptics and disinfectants, various devices for curing influenza, and malaria remedies deficient in cinchona alkaloids. Paralysis from the consumption of ginger products containing orthocresyl phosphate led to seizures and jail sentences for conspiracy to violate the Act. The government lost an action against Banbar for the treatment of diabetes, orally. Sales of dinitrophenol were continued in spite of the warnings of danger of using it to produce loss in weight. A "cancer serum" containing tetanus toxin caused 12 deaths before it could be removed from the market. The highlight of 1938 was the action against a company for distributing 240 gallons of sulfanilamide in diethylene glycol, which was responsible for over a hundred deaths; almost the entire field force was brought into this campaign and 99.2 per cent of the total quantity was collected. At the same time the decisions of the courts were helpful in planning projects for further drug control. Experience gained in the enforcement of the 1906 Act revealed a number of shortcomings. Efforts were started about 1933 to strengthen it or replace it. Bills were offered annually until finally the proposal of Senator R. S. Copeland of New York was passed and signed by President Franklin D. Roosevelt on June 25, 1938. This is known as the Federal Food, Drug, and Cosmetic Act. This new Act retained the useful features of the 1906 Act, but established separate sections dealing with food, with drugs and devices, and with cosmetics.

Provisions of 1938 Act

Section 201(g) extends the term "drug" to include articles in the official *Homoeopathic Pharmacopoeia* of the United States. It expands the scope to include articles intended for use in the diagnosis, mitigation, treatment, cure or prevention of disease in man or other animals. It includes articles intended to affect the structure or any function of the body. Section 201(h) defines "devices" as instruments, apparatus and contrivances for the same purposes. Section 201(o) requires that an antiseptic shall be a germicide, except when it is represented as an inhibitory product. A new subsection (p) was added to define "new drugs":

(p) The term "new drug" means—

(1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the

enactment of this Act it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug the composition of which is such that such drug, as a result of investigations to determine its safety for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

Section 301 extends the prohibitions of the previous Act to cover devices and cosmetics. Section 301(k) also prohibits the alteration, multilation, destruction, obliteration or removal of the whole or any part of the labeling of, or doing any other act with respect to, a drug, while held for sale (amendment following the *Sullivan* decision—"whether or not the first sale") after shipment in interstate commerce, which would cause the article to be adulterated or misbranded. Penalties for violation of Section 301 were increased to a fine of not more than $1,000, or imprisonment for one year, or both; however, for a second or subsequent offense, or for any conviction with intent to defraud or mislead, fines not to exceed $10,000 and imprisonment for not more than three years, or both. Section 304 provides for seizure of offending materials.

Chapter V is restricted to drugs and devices. Section 501 defines adulteration; Section 502, misbranding; Section 503, exemptions; Section 504, coal-tar colors; Section 505, new drugs; Section 506, certification of insulin; and Section 507, certification of certain antibiotics. Section 502(f) requires the labeling to bear adequate directions for use, and warnings against use in pathological conditions or by children where such use may be dangerous to health, or against unsafe dosage or methods or duration of treatment. Based on safety, Section 503 was amended by the Durham-Humphrey Amendment, requiring habit-forming or toxic drugs to be restricted to dispensing on prescription and at the same time prohibiting the dispensing of safe drugs on prescription. Section 505 outlines the method of obtaining reports of investigations on the safety of a new drug, listing the composition, method of manufacture and control, and filing of labeling for use with any new drug, also provisions for transferring drugs from prescription to over-the-counter sale.

Sections 601 to 604 deal with cosmetics. Sections 701 to 706 include general regulations, hearings, examinations, sea-food and factory inspection, and publicity. Imports and exports are considered in Section 801. Various amendments to the 1938 Act have been adopted, usually following court decisions in contested cases.

Data published in the annual reports for the fiscal years 1940 through 1954, or 15 years, may be contrasted with those, above, for 1907 through 1939, with respect to enforcement statistics. For these 15 years, the percentage of time spent in the drug area ranged from 23 per cent in 1947 to 41 per cent in 1954, and averaged 29 per cent. The drug imports refused during this interval totaled 19,800 out of 50,006, or 40 per cent. Drug prosecutions totaled 4,552 out of 15,396, or 30 per cent; and seizures, 6,302 out of 33,803, or 19 per cent. The publication of N. J.'s was continued under authorization of Section 705, but classified into three types. As of June 1, 1956, there have been published 22,300 N. J.'s dealing with food, 4,600 on drugs and devices and 202 on cosmetics. With respect to new-drug applications, there were 1,277 filed during 1939 and 1,475 during 1940; a total of 5,300 by 1944; and over 10,000 by May, 1956.

Summary of Actions Under 1938 Act

These reports indicate continued study of headache remedies, dental and veterinary products, vitamins, venereal remedies, diabetic preparations, abortifacient pastes, pyrogens, glycols, hormone preparations and antibiotics. The safety of boric acid preparations, coal-tar colors, coumarin and synthetic sweetening agents have been investigated in detail. Campaigns were started against "pitchmen" or "spielers" for oral misrepresentations in the sale of properly labeled preparations. Campaigns were undertaken against the fringe minority of the pharmacists who refilled prescriptions for barbiturates, stimulants and thyroid preparations without physicians' permission, or for selling such products over the counter without prescription, caution or warning. In the early days, fines were imposed and, later, jail sentences were inflicted on the few continuing violators. Information in these annual reports has been supplemented in certain areas by N. J.'s under the 1938 Act:

(1) N. J. D. D. (Drugs and Devices) 2254: The action in *U. S. v. J. J. Sullivan* originated in the district court in Georgia in 1946 because of the sale of sulfathiazole tablets over the counter without a prescription, warning, caution, or directions for use. The tablets were removed by the druggist from a properly labeled large bottle, and his sale was intrastate. The district court decided that federal authority extended to control labels on drugs which had moved interstate until they reached the ultimate consumer; upon return of a verdict of guilty, a fine of $200 and two years' probation was imposed. On appeal, the

Circuit Court of Appeals for the Fifth Circuit reversed this decision, holding that Section 301(k) applied only to the first sale by a person who received any interstate shipment. This decision was reversed by the United States Supreme Court (332 U. S. 689) on January 19, 1948, with the statement that Congress prohibited misbranding of products held for sale after shipment in interstate commerce, all the way to delivery to the ultimate consumer, and that these tablets were not labeled as required by the 1938 Act; therefore, Sullivan was guilty. To remove any possible doubt, an amendment to Section 301(k) was then adopted by inserting the clause "(whether or not the first sale)."

In N. J.'s D. D. 3967-3968, *U. S. v. Sanders,* the defendant had been enjoined from interstate shipment of a misbranded drug preparation (a mixture of ground hoof and horn in milk) for the cure of arthritis, cancer and diabetes. However, he continued to sell this product to persons coming to his home, even though he knew they came from other states. The district court held that the defendant was not engaged in interstate commerce. The United States Court of Appeals for the Tenth Circuit reversed this decision, stating that the 1938 Act prohibited not only introduction of misbranded drugs into interstate commerce, but also delivery for introduction into interstate commerce, since that included purchase and transportation.

(2) In N. J. D. D. 1231, *U. S. v. "666,"* the original product contained quinine, among other drugs; during the shortage associated with World War II, quinine was called in by the government, and was unavailable. The manufacturer continued to make the product without quinine, packaged in a container and carton with figures similar to those previously used. Even though the purchaser reading the label would not be misled, the jury agreed with the contention of the government that the product would be misleading.

(3) Two courts ruled on the establishment and use of tolerances. (a) N. J. D. D. 996, in *U. S. v. Double Strength Posterior Pituitary Solution,* held that the tolerance for the *United States Pharmacopoeia* 10-unit solution did not apply to the nonofficial 20-unit product. (b) Examination of prophylactics in N. J. D. D. 2276 indicated 7 per cent-11 per cent of defectives in samples tested. In overruling the defense claim that the samples represented only 1 per cent of the total shipment, the court ruled that it was not required to establish any tolerance or sampling formula in this connection.

(4) In N. J. D. D. 917, *U. S. v. Buffalo Pharmacal Company and J. H. Dotterweich,* misbranding was charged, since digitalis showed

less than half of the labeled potency, and Hinkle Pills still contained strychnine, which ingredient had been deleted in the present *National Formulary* formula. The jury held the company not guilty, but returned a verdict of guilty against Dotterweich as an officer of the company. This decision was reversed by the Circuit Court of Appeals for the Second Circuit. On appeal, the United States Supreme Court decided (320 U. S. 277) on November 22, 1943, to reverse the court of appeals, holding that a jury can find any officer of a corporation guilty even though it fails to convict the corporation. Whether all persons who aid and abet in the commission of a crime within a corporation are equally guilty is a fact which must be decided by the jury. This decision led to a number of subsequent actions jointly against a corporation and one or more of its officers.

(5) The question of a suitable judicial definition for the term "accompany" used in Section 201(m) ("The term 'labeling' means all labels and other written, printed, or graphic material . . . accompanying such article") was the basis for a number of actions; the decisions were not always in agreement. Among these, the following are selected as typical:

N. J. D. D. 92, *U. S. v. Rakos et al.*—for a poultry remedy. A district court decided that booklets shipped ahead of the product—but displayed with it when sold—did "accompany" the drug.

N. J. D. D. 376, *U. S. v. "Electreat Mechanical Heart"*—the district court ruled that the accompanying literature contained misleading claims and that the device could not be used without the directions contained in that literature.

N. J. D. D. 821, *U. S. v. Royal Lee,* covered therapeutic claims for vitamin products. The complaint that the literature containing false claims—shipped interstate separately from the product, but displayed with it while held for sale—was labeling but did not accompany the drug led the district court to dismiss. On appeal, the Circuit Court of Appeals for the Seventh Circuit reversed this decision, ruling that the circular was misbranded, and did accompany the drug.

N. J.'s D. D. 829, 2375, 3310, 3363, 3767, and many others, *U. S. v. Alberty's Foods*—a number of actions were taken in the various courts against a large number of drug products of various compositions advocated for many types of disease. It was held that booklets did accompany these articles (N. J. 829), since both the circulars and the

drugs had a common source and a common destination and were displayed together, even though the leaflets had been shipped 71 days before the drug in some instances (N. J. 2375). A circuit court decision reversing was, in turn, overruled by the United States Supreme Court. It was further held that the labeling did not contain adequate directions for use, since it did not state all of the diseases or conditions for which it was offered to the public, and also that a previous Federal Trade Commission cease-and-desist order did not prevent FDA action on charges of misbranding.

N. J. D. D. 1380, *U. S. v. Nue-Ovo*—in this proceeding the district court ruled that the product and the circulars came from a single shipper to a single consignee, so the circulars accompanied the products. The Circuit Court of Appeals for the Ninth Circuit reversed the lower court, and the Supreme Court denied certiorari, so the case was retried by the district court. This time the jury reached a verdict that the product was useless in the treatment of arthritis, and destruction was ordered.

In N. J.'s D. D. 1584-1585, *U. S. v. Boncquet Tablets,* the district court dismissed as moot an action against a shipment of dried brewer's yeast and circulars claiming value for certain disease conditions, since none had been distributed over the past two years. The Circuit Court of Appeals for the Fourth Circuit reversed this decision, ruling that circulars shipped separately from the drug, but designed for use by dealers in its sale, did accompany the drug under this section, also that continued compliance does not relieve goods of liability for past actions while condemnation is unheard.

N. J. D. D. 2473, *U. S. v. Kuriko*—statements in a pamphlet wrapped around the bottle could be misleading.

N. J. D. D. 2578, *U. S. v. Drs. Kaadt*—a combination of potassium nitrate and diastase in vinegar was sold for the treatment of diabetes. The jury found both defendants guilty, and a fine of $1,000 and three years in jail were imposed on each. Testimonials by laymen stating that the product was effective were quoted in circulars; expert physicians said it was not. The circular containing the claims was not directly associated with the drug, but was "labeling." The verdict was upheld on appeal to the United States Court of Appeals for the Seventh Circuit.

N. J. D. D. 2555—In *U. S. v. "Tox Eliminator,"* a district court held that pamphlets and letters shipped from California to Oklahoma

were necessary labeling, since there was only a name plate on the device; therefore, they accompanied it by "commercial association." Otherwise, there were no adequate directions for use of the device.

N. J. D. D. 2580—In *U. S. v. Kordel,* it was ruled in the district court that the literature, pamphlets, circular and display card came from the same origin to the same consignee and, therefore, did accompany the drug, even though not shipped in the same container. The verdict of guilty was affirmed by the Circuit Court of Appeals for the Seventh Circuit. To clarify several conflicting decisions in the lower courts, this was reviewed by the United States Supreme Court on November 22, 1948. It held that since the drugs and the literature had a common origin and destination and since the literature was used to sell and explain the use of the drugs, it did "accompany" the products.

N. J. D. D. 3058, *U. S. v. Fred Urbeteit* (sinuothermic devices)—this case was based upon the shipment of a small newspaper, carrying testimonials from patients and information regarding use of a machine, to one of the pupils trained under Urbeteit. Since part of the devices were shipped three weeks before the newspapers and the remaining units three weeks after the newspapers, the question arose as to whether they "accompanied." The district court held that they did; the Circuit Court of Appeals for the Fifth Circuit held that they did not. This was appealed to the United States Supreme Court in conjunction with the *Kordel* case and it was decided on November 22, 1948, that since these leaflets explained the usefulness of the device, and the movement of the machine and the leaflet was a single, interrelated activity, these leaflets were accompanying labeling.

N. J. D. D. 3457, *U. S. v. Color-Therm*—instructions written in Kansas were mailed to distributors in Oklahoma, who recopied them and placed a folded copy in each device at the time of delivery. The decision of the district court was upheld by the Circuit Court of Appeals for the Tenth Circuit, that these instructions did accompany the device, even though not physically attached to it. Once a device is misbranded, it is subject to seizure at any time, even without a false label.

N. J. D. D. 3658, *U. S. v. Blackstrap Molasses*—in connection with the sale of this properly labeled product, the vendor displayed a book *Look Younger, Live Longer,* which discussed the action of the product in a number of disease conditions. The court held that the act of showing these to the purchaser made the book "accompany" the product.

N. J. D. D. 4029, *U. S. v. Ruth D. Drown*—the verdict of the district court that the devices involved herein were misbranded was affirmed by the United States Court of Appeals for the Ninth Circuit. The Supreme Court denied certiorari. Commerce includes purchase and transportation, and the place of passage of title is not significant. Labeling includes materials sent to the purchaser subsequent to sale, where the transaction is integrated. Even if adequate directions for using a harmless device are given, there is a possible danger in its use that the ignorant or gullible will rely on it instead of seeking professional advice.

(6) A number of decisions dealt with misbranding by improper or excessive therapeutic claims, usually with the indication that no product or combination of products would be capable of producing the effects specified. Typical decisions are noted:

N. J. D. D. 513, *U. S. v. Merlak Mineral Water*—if there is a material weight of scientific evidence contrary to representations in labeling, which is not mentioned therein, this omission constitutes misbranding.

N. J. D. D. 1010, *U. S. v. Howard-Iowa Products*—this product was specifically labeled for use in the treatment of *Ascaris* in hogs. The district judge dismissed the government contention that this product was making the claim, in effect, that it was a cure or treatment for *all* species of worms infesting hogs.

N. J. D. D. 1251, *U. S. v. Marmola Tablets*—one of the charges was that the presence of 0.5 grain of thyroid per tablet, with a recommended dose of four tablets per day, if taken without medical examination, made this inherently dangerous to the strong and weak, the old and young, the well and sick. The district judge indicated that any drug which, for safety of use, requires diagnosis and evaluation and which may cause disease when taken in accordance with the label is dangerous to health and is unsafe for self-medication for obesity. This opinion was affirmed by the Circuit Court of Appeals for the Seventh Circuit, and the United States Supreme Court denied certiorari. The recommended product does not need to be dangerous to the health of all persons who take it at the dosage, and for the duration, suggested; the product is misbranded if represented as safe.

N. J. D. D. 1980, *U. S. v. Paddock*—advertising matter may also be labeling; it is not possible to evade the law by placing advertising

matter in the hands of purchasers before buying the product. A permanent injunction was granted against shipping misleading circulars by mail with the drug—or prior or subsequent thereto—intended to be used by the purchaser in accordance with the method of treatment for gall stones recommended therein.

N. J.'s D. D. 2389-2390, *U. S. v. Dinshah P. Ghadiali and Spectro-Chrome Institute*—a large number of seizures were made of this device, consisting of colored glass slides for diagnosis and treatment of a very large number of diseases. Among these seizures was one involving removal from a private home of a machine with which the purchaser was satisfied, under the theory that after a misbranded device has passed into interstate shipment it may be proceeded against at any time; the right of a person to prescribe for himself is subordinate to the right of the government under Section 304.

N. J.'s D. D. 3381-3383, *U. S. v. Mytinger & Casselbury* (Nutrilite)—multiple seizures were made of this drug product because the Federal Security Administrator believed its labeling might materially mislead to injure or damage the purchaser or consumer; no hearing had been held prior to the seizures. Reversing the lower courts, the United States Supreme Court (CCH FOOD DRUG COSMETIC LAW REPORTS ¶ 7156, 339 U. S. 594) ruled that this was not necessary, since a hearing could be held before issuance of the final order. The purpose of the multiple seizures was to arrest distribution of the article pending determination of adulteration or misbranding. Consolidation of the multiple libel suits into a single trial is the relief offered distributors. In settling this case, allowable claims for the product involved were specified in some detail. It was also ruled that the labeling must enumerate all of the purposes and conditions for which the articles are intended to be used, together with proper directions for such multiple uses.

N. J. D. D. 4100, *U. S. v. Phonograph Records*—in considering the charge of false therapeutic claims for the treatment of insomnia by hearing certain records, the district court held that they were not devices, under the 1938 Act. The United States Court of Appeals for the Second Circuit reversed this decision, stating that they were components of a phonograph, and claimed to affect sleep, which is a function of the body; therefore, they were "devices."

(7) A number of decisions were based on the lack of adequate directions for use on products, and the question as to whether or not

they might be considered as dangerous to health if taken in accordance with directions; in some instances, there were no warnings. Such decisions include:

N. J.'s D. D. 1001-1002, *U. S. v. Sekov Corporation*—extending the decision in the *Marmola* case, the district court held that this thyroid extract reducing product was dangerous to health when used as prescribed in the labeling and was being sold directly to laymen without medical examination. The directions were not adequate, since it would be dangerous to use as directed on the label. This decision was affirmed by the Circuit Court of Appeals for the Fifth Circuit.

N. J.'s D. D. 1040, 2922, 3061, and many others, *U. S. v. Colusa Natural Oil*—this crude petroleum product, containing small amounts of other ingredients, was improperly recommended for the treatment of psoriasis and other skin diseases, and for piles and hemorrhoids. The jury returned a verdict of guilty in the district court. Since the judge had barred testimony by experts for the defendant during the presentation of the case, the finding was reversed, and the case remanded for retrial. Interstate shipment was forbidden by injunction, since no adequate directions for use were given for treating the various conditions recommended in the advertising, which went far beyond the statements on the label. This seizure was approved by the district court and affirmed by the United States Court of Appeals for the Eighth Circuit; the United States Supreme Court denied certiorari. It was held that the statement "for use in the treatment of" implied that a product was useful in the treatment of the diseases listed. This case did not involve a mere difference of opinion between various medical schools, but the question was whether this drug would be effective in curing, or giving relief from, the diseases for which it was recommended.

N. J. D. D. 1157, *U. S. v. Arner,* involved the shipment of some 100,000 tablets in bulk in drums, without directions for use, or warnings or cautions. The decision of the district court that this container was improperly labeled and, therefore, should be seized was affirmed by the Circuit Court of Appeals for the First Circuit. Such information is required not only for the ultimate purchaser, but also as evidence of compliance with the requirements of the Act by the shipper.

N. J. D. D. 2355, *U. S. v. W. K. Hassenstein, Rx 5,000*—this product contained cotton-root bark, ergotin, aloes and oils of pennyroyal and savin, apiol and posterior pituitary extract. In one case a judge dis-

missed the information on the basis that the statements "to be used as directed by physician, not to be used by children" constituted adequate directions for use. Another court granted perpetual injunction against interstate shipment under the same conditions and labeling.

N. J. D. D. 2405, *U. S. v. Bush Mulso, et al.*—the court ruled that a combination of papain, charcoal, alfalfa and kelp was a drug, since it was recommended for the treatment of neuritis. The labeling did not contain adequate directions for use, since the labels did not inform the customer of the conditions for which the product was intended.

N. J. D. D. 3550—in *U. S. v. El-O-Pathic Pharmacy,* the district court denied the government request for injunction to restrain interstate commerce in certain hormone drugs since the labeling did not bear adequate directions for use, and they were being resold without prescription, although the original labeling suggested consultation with a physician before use. The court held that these drugs were not dangerous to health when used in accordance with instruction by the physician and, therefore, carried adequate directions. This decision was reversed by the United States Court of Appeals for the Ninth Circuit after expert witnesses showed that these products were inherently dangerous drugs and that labeling showing adequate directions for unsupervised use could not be written. Adequate directions for use must include every disease for which the product is proposed. If the product is safe only on the advice of a physician, the label may require that the product be taken only on prescription.

In N. J. D. D. 3567, *U. S. v. Halox,* a device for the electrolysis of sodium chloride solution was seized because it did not have adequate directions for use; the court ruled that devices were not exempt from these requirements since adequate directions were not readily available.

In N. J. D. D. 4047, *U. S. v. Basic Endocrine Sales,* seizure was approved by the district court because the product did not carry adequate directions for use. The label stated that the product was to be used only under the direction of a doctor. There was no scientific evidence of the value of the product following oral administration, although it had been sold for 17 years.

N. J. D. D. 4327, *U. S. v. Tryptacin Tablets*—in approving a decree of condemnation and destruction, the district judge held that advertising was a part of the labeling. In this case, the ads claimed that the

product would cure gastric ulcers within four weeks, although there was no mention of ulcers on the label; hence, it was misbranded.

(8) Decisions have been handed down in a number of courts that testimonials by laymen are not persuasive as contrasted with conflicting medical evidence and testimony; that alterations in symptoms may be presented by lay witnesses, but they are prohibited from concluding that these changes are the necessary result of the medication taken. It is not necessary that qualified experts have personal experience with a drug or device in order to express expert opinions regarding its merit. While the courts have recognized differences in medical opinion, there are certain areas in which these differences are not honest differences of opinion regarding effectiveness. (N. J. D. D. 345, *U. S. v. Heron;* N. J. D. D. 375, *U. S. v. Kahng;* N. J. D. D. 2921, *U. S. v. Research Laboratories;* N. J. D. D. 2963, *U. S. v. Nue-Ovo;* N. J. D. D. 2987, *U. S. v. Radiant Ozone Generator;* N. J. D. D. 3017, *U. S. v. "Tox Eliminator";* N. J. D. D. 3177, *U. S. v. Chloresium Toothpaste;* N. J. D. D. 3436, *U. S. v. Vrilium.*)

(9) Typical decisions showing the wide scope of the 1938 Act include:

In N. J. D. D. 605, *U. S. v. Mrs. Moffat's Shoe Fly Powders for Drunkenness,* the product contained 3.2 grains of tartar emetic per powder, as contrasted with the usual dose of 0.05 grain (death has been reported following ingestion of two grains). Physicians testified that they had studied this article and found it to be dangerous to health. The defense testified that the sale of the product had exceeded 50,000 packages per year for the preceding ten years. The district court found the product to be dangerous and ordered its destruction.

N. J. D. D. 725—a permanent injunction was granted against interstate shipment of Diaplex, an infusion of eight tablespoonfuls of saltbush, *Atriplex canescens,* in two quarts of water daily, for the treatment of diabetes. This was but one of many herbal products proposed for oral administration in the treatment of diabetes.

N. J. D. D. 2468 reports a case involving the mixture of stramonium with peppermint, boneset and belladonna leaves. In response to a plea of *nolo contendere,* the court imposed a fine of $2,300 and costs against the company, and $200 and costs against the individual who was the president.

N. J. D. D. 2656 reports a suit to enjoin shipment of a number of different solutions because of the presence of substantial quantities of undissolved material therein. A series of interrogatories were answered as the basis for the trial in January, 1949. On the basis of the testimony, the court dismissed the request, since the standards were too indefinite and the evidence presented was insufficient to show violations of the 1938 Act. This led to a prolonged cooperative investigation for the development of electronic devices to determine undissolved particles and also to a change in the requirements of the *United States Pharmacopoeia.*

N. J. D. D. 2756 reports a case involving the use of a noncertified coal-tar color, "butter yellow (dimethylazobenzene)" in a drug product, also failure to declare the common or usual name for one of the ingredients. The district court returned a verdict of guilty, with a fine of $1 against the company and fines of $500 against each of its two officers. On appeal, the United States Court of Appeals for the Third Circuit reversed the decision regarding the name, and remanded for retrial. The jury returned a verdict of guilty on the dye charge, with fines of $100 against the company and of $150 and $100 against the individual officers.

N. J. D. D. 3201 involved distribution of a 2 per cent solution of procaine hydrochloride containing an excessive quantity of hydrochloric acid which caused damage when used in dental practice, also a vitamin product which was deficient in potency. Prosecution was brought for both misbranding and adulteration. It developed that the company was not making laboratory tests to control the amount of hydrochloric acid in the finished product. The corporation and two of its officers pleaded *nolo contendere.* The district court stated that the officers of a corporation must bear the penalties, as well as enjoy the benefits, of their office; penalties were inflicted to remind all parties of the need to exercise the strictest care in the preparation of drug products. A fine of $1,800 was imposed on the corporation, and fines of $1,800 and $900 upon the officers.

N. J.'s D. D. 3652 and 3770 involved interstate shipment of a-estradiol tablets which were substandard, assaying 23 per cent to 68 per cent of labeled potency. The defense offered was that the method of analysis in *United States Pharmacopoeia XIV* was unsatisfactory. The court held that the distributor of a drug product had the liability

of insuring conformity to labeled potency declaration; since these shipments were made before the product was recognized in *United States Pharmacopoeia XIV,* there was no restriction to the method therein, but any method of assay could be used. The district court imposed fines of $2,500 against the company and $500 against each of two officers. This was affirmed by the United States Court of Appeals for the Ninth Circuit.

N. J. D. D. 4094—therapeutic claims were made that Fairfax Cigarettes would prevent respiratory diseases, colds, influenza, pneumonia, tuberculosis and parrot fever. The district judge ruled that the use of these claims rendered the product a "drug" under the Act.

N. J. D. D. 4351—during the process of transferring gases from large to small cylinders, carbon dioxide was placed in a cylinder labeled as containing oxygen. Upon pleas of guilty, fines of $750 and $150 were imposed on two of the company's officers, and jail sentences of six months and of three months were suspended.

It may be noted from this summary of actions under the 1938 Act, as amended, that the extent of enforcement has been materially broadened. A greater degree of personal responsibility is being required of the officers and technical men of corporations. It may also be noted that there has been a progressive increase in the complexity of problems associated with the production, packaging and distribution of drugs, drug products and devices.

Half a century ago adulteration of drugs with dirt or foreign material was not uncommon; products were improperly collected or handled, and fell below labeled potency. Mixtures of foreign substances with synthetic drugs were often encountered, although synthetics were just starting to become widely used and to displace crude drugs. The recognition of the official compendia (the *United States Pharmacopoeia,* the *Homoeopathic Pharmacopoeia* and the *National Formulary*) introduced measuring sticks for determining quality, purity and strength; this resulted in definite improvement in the official products. The development of hormones, of antibiotics and of products of synthetic origin during the last 50 years has been paralleled by the development of monographs covering the products. The early activity of the Council on Pharmacy and Chemistry of the American Medical Association in providing standards for new and nonofficial remedies has been replaced to a substantial degree by the new-drug requirements under Section 505 of the 1938 Act, with respect to quality, purity and strength of such products.

The sweeping and widespread claims of the vendors of patent and proprietary medicines 50 years ago, as reported in *Nostrums and Quackery* and in "The Great American Fraud" and similar statements, has largely disappeared. Much of this improvement has been developed by the industry itself. The codes of ethics of the various drug-manufacturing associations have led to tightening the privilege of obtaining and maintaining membership in these associations. The labels, labeling, advertising and radio and television copy and other media for bringing the merits of drug preparations to the attention of the member of the medical profession, the veterinarian, the dentist, the pharmacist, the nurse or the lay consumer have all been scrutinized thoroughly and continuously. Scientific investigations have been planned and conducted to support therapeutic claims not only for old drugs, but also for new drugs which are constantly appearing on the market.

Improvements in research methods have led to more fundamental studies of the metabolism of drugs—not only to determining what the drug does to the body, but to how it produces its effects, and to determining the transformations of drugs within the body. Increasing knowledge of the mechanisms of disease and of drug action help to develop information on the proper role of any product in the treatment of any disease, recognizing limitations as well as possibilities; side effects and their prevention; toxicity; and other factors not capable of investigation 50 years ago.

Fewer than 10 per cent of the present prescriptions could have been filled 50 years ago, because the ingredients were unknown or unavailable. This same progress may be expected to continue with further researches. In 1906, the population of the United States was about 85 million; now it is about twice that number. At that time, the total value of drug preparations may be estimated at about $100 million at the manufacturers' level; now it could be estimated at 15 times that level. At that time there was little general knowledge of diseases and therapy among the laymen; the development of articles about these subjects is now commonplace in practically all types of magazines. The improvement in methods of scientific research on the nature and prevention of disease, as well as the production of specific therapy during the last half-century, has enlarged the available therapeutic armamentarium, and permitted more specific and comprehensive development of drug control. **[The End]**