Besides separate certificates in bacteriology, serology, biochemistry, and parasitology, one all-inclusive certificate, called Senior Clinical Laboratory Technician, will be issued by examination, which certificate entitles its holder to be licensed to engage in all the work of a clinical laboratory.

10. All persons believing themselves eligible to receive any sort of license without examination should immediately write to the State Division of Laboratories, Berkeley, requesting forms on which to apply for the license. Owing to the short time remaining before January 1, where it appears impossible to complete the necessary investigation preliminary to the issuance of a license, a temporary license revocable at any time will be issued.

Such temporary licenses must be replaced by permanent licenses before July 1, 1938.

11. Fees. (Rule 14 of regulations.)

(a) *Clinical Laboratory Technologists.*—The fee for the certificate of license as clinical laboratory technologist shall be $10, payable with application for license without examination. If the applicant is found ineligible, the fee will be returned. The fee for examination for the certificate as clinical laboratory technologist shall be $5, payable with application, and not returnable in case of failure. If the applicant passes, an additional $5 must be paid before the certificate is issued. The annual renewal fee for license as clinical laboratory technologist shall be $10 for each year following the calendar year in which the certificate was issued, and payable within sixty days after the commencement of each calendar year.

(b) *Senior Clinical Laboratory Technicians.*—The fee for the examination and the certificate as senior clinical laboratory technician shall be $5, payable with application, and not returnable in case of failure. The license as senior clinical laboratory technician is good for the remainder of the calendar year in which issued, and must be renewed annually by the payment of a fee of $2 within sixty days after the commencement of each calendar year. A certificate as senior clinical laboratory technician will be issued without examination, but on the payment of the fee of $5, to all persons holding the four certificates of proficiency (Senior Grade in the old series) issued by the Board. In cases where an examination has been paid for in the securing of individual certificates, credit for such payments will apply on the fee for the issuance of the full certificate as senior clinical laboratory technician.

(c) *Certificates of Proficiency.*—These certificates, one in each of the subjects of bacteriology, serology, biochemistry, and parasitology, will be issued by examination in these subjects separately. The fee for the examination in any one subject and for the certificate and license good for the remainder of the calendar year is $2, not returnable in case of failure.

Persons now holding one or more certificates of proficiency will be issued licenses for the activities covered by the certificates which they hold. If an application for license without examination is filed, it may be found possible to include in the license issued other activities not covered by the certificate of proficiency held by the applicant.

A license in parasitology is given only by examination. The license as senior clinical laboratory technician is not given without examination except to holders of four certificates.

12. The law does not require technicians working in a doctor's office to be licensed unless work is done for other doctors or for the patients of other doctors.

13. The exemption of nonprofit hospitals, provided for in Section 6 of the law applies only to hospitals maintained by corporations for the benefit of their own employees, the hospitals being supported by "dues or contributions from employees of a common employer, or a group of affiliated employers. . . ."

14. The renewal fee for certificates of proficiency is fifty cents each, payable annually. A pocket license card is issued upon payment of the fee. Renewals and licenses for 1938 will be ready for distribution early in November.

15. Holders of four certificates of proficiency may exchange them for a senior clinical laboratory technician's certificate, or, if they meet certain other requirements, for a technologist's license.

ELIXIR SULFANILAMIDE—MASSENGILL*

Report of the United States Secretary of Agriculture

During September and October of 1937 at least seventy-three persons died as a direct result of taking the drug known as "Elixir Sulfanilamide." Twenty other persons who took the "elixir" died, but it has not yet been established that this drug was exclusively responsible. The ninety-three deaths occurred in fifteen states, as far east as Virginia, as far west as California.

"Elixir Sulfanilamide" was manufactured and sold by the S. E. Massengill Company of Bristol, Tennessee. According to the firm's books, 240 gallons were manufactured. The entire amount has been accounted for.

Before the "elixir" was put on the market, it was tested for flavor but not for its effect on human life. The existing Federal Food and Drugs Act does not require that new drugs be tested before they are placed on sale.

"Elixir Sulfanilamide" was first distributed commercially on September 4, 1937, and continued to October 15, 1937. The first word of deaths from an unidentified sulfanilamide preparation reached the Food and Drug Administration on October 14. On October 16 an investigator for the Administration telegraphed from Tulsa, Oklahoma, that nine persons had died there after taking "Elixir Sulfanilamide." Seizure of all outstanding shipments was immediately ordered.

Since the Federal Food and Drugs Act contains no provision against dangerous drugs, seizures had to be based on a charge that the word "elixir" implies an alcoholic solution, whereas this product was a diethylene glycol solution. Had the product been called a "solution," rather than an "elixir," no charge of violating the law could have been brought.

Of the 240 gallons manufactured, 228 gallons and 2 pints have been seized under federal and state laws, destroyed, collected as laboratory samples, or wasted by spillage and breakage. Eleven gallons and six pints were dispensed on prescriptions or over-the-counter sales. Of this amount, about half was consumed and caused the deaths; the other half was retrieved before consumption.

The lethal effect of the "elixir" was due to its content of diethylene glycol, which was used as a solvent in making a liquid preparation of sulfanilamide, usually administered in tablet or powder form. Sulfanilamide itself is a valuable drug, and was not responsible for the disaster.

Sulfanilamide is the name of one of a group of closely related chemicals first reported in European medical literature of 1935 to have been used for drug purposes. It has shown dramatic curative effects. Physicians in this country have been quick to recognize its far-reaching possibilities. Its use has grown to tremendous proportions. An editorial from the *Journal of the American Medical Association* stated that sulfanilamide is potentially dangerous, but that properly used it may be brilliantly successful in treating various infections.

The fatal "elixir" was rushed onto the market without adequate test to determine whether or not diethylene glycol may be safely used as a solvent for sulfanilamide, despite previously published reports in scientific literature showing that diethylene glycol might be dangerous when taken internally. A few simple and inexpensive tests on experimental animals would have quickly demonstrated the toxic properties of both diethylene glycol and the "elixir."

It will be observed that the preparation is a semi-secret one, that the presence of diethylene glycol is not disclosed, and that no warning of danger appears.

Most of the drug was administered on physicians' prescriptions.

HOW THE "ELIXIR" WAS PRODUCED

For some time before putting "Elixir Sulfanilamide" on the market, the S. E. Massengill Company had been marketing sulfanilamide in capsule and tablet form. In June, 1937, the firm's salesmen reported a demand for the drug in liquid form. Near the end of July, Mr. Watkins,

* Submitted to Congress at Washington, D. C., in response to House Resolution 352 of November 18, 1937, and Senate Resolution 194 of November 16, 1937.

See also editorial comment in December CALIFORNIA AND WESTERN MEDICINE, on page 366. For list of United States Senators and Representatives, to whom letters may be sent, in favor of revision of Federal Food and Drug laws, see in this issue on page 71.

chief chemist of the Massengill Company, according to his own statement, undertook the problem of finding a suitable liquid vehicle for sulfanilamide. Since sulfanilamide is insoluble in the various liquids commonly employed in making medicines, he tried a number of other solvents. Diethylene glycol was found to dissolve as much as 75 grains of sulfanilamide per fluidounce, but in that concentration it tended to separate out on chilling. Accordingly he decided upon 40 grains per fluidounce as a stable preparation and devised the following working formula:

Sulfanilamid	58½ pounds
Elixir Flavor	1 gallon
Raspberry Extract	1 pint
Saccharin Soluble	1 pound
Amaranth Solution 1-16	1½ pints
Caramel	2 fluidounces
Diethylene Glycol	60 gallons
Water q. s.	80 gallons

According to Mr. Watkins no tests were made to determine the toxicity of either the separate ingredients or of the finished product, or to determine by well-known methods available for the purpose whether or not the sulfanilamide decomposed in the diethylene glycol. The so-called control laboratory merely checked the "elixir" for appearance, flavor, and fragrance. Doctor Massengill confirmed Mr. Watkins' statement that no experimental animals were used or clinical tests of any kind made to determine either the effectiveness or the toxicity of the drug before it was put on the market.

THE FOOD AND DRUG ADMINISTRATION STEPS IN

The first word of deaths from an unidentified sulfanilamide preparation reached the Food and Drug Administration on October 14, 1937, through a telephone call from a New York physician associated with a large drug manufacturing concern. He repeated advices, presumably received through professional or trade contacts, that fatalities had occurred at Tulsa, Oklahoma.

Immediately instructions to investigate the report were issued by telegraph to the Kansas City station of the Food and Drug Administration, which is the nearest station to Tulsa. A representative of the Administration arrived in Tulsa the following day. He reported by telegraph on Saturday, October 16, that nine deaths had already occurred in Tulsa, including eight children with streptococcic sore throat and one adult with gonorrhea, and that all had taken a product labeled "Elixir Sulfanilamide. The S. E. Massengill Company, Manufacturing Pharmacists, Bristol, Tennessee."

Shipping records showed that the suspected "elixir" had come from a Massengill establishment in Kansas City, to which the station immediately sent inspectors. Also an inspector from the Cincinnati station, which is the nearest station to Bristol, and a medical officer from the Administration's headquarters at Washington, were sent at once to Bristol.

It was found that some of the "elixir" had been made at the Kansas City branch factory and that supplies had been sent to the New York and San Francisco sales branches. Immediately inspectors from the New York and San Francisco stations were assigned to investigate distributions from these points.

It was learned that the Massengill Company, following reports of the poisonous effects of the "elixir," had sent out approximately 375 telegrams from Bristol and additional telegrams from its branch houses totaling, according to the firm's statement, some 1,100 in all, requesting the return of outstanding shipments.

On or about October 15, on telegraphed instructions from the Bristol office, the San Francisco branch of the firm instructed its salesmen to have outstanding stocks returned. However, investigation revealed that no attempt had been made by that branch to communicate directly with dealers and doctors.

The telegrams and letters sent out by the Massengill Company gave no indication of the dangerous character of the product and were not calculated to impress receivers with the emergency character of the call for returning the goods, the inspector assigned to the Bristol office insisted that the firm issue the following telegram, dated October 19, to all persons who were listed as having received shipments of the "elixir" from Bristol:

Imperative you take up immediately all Elixir Sulfanilamide you dispensed. Product may be dangerous to life. Return our expense.

Following similar insistence by the San Francisco, Kansas City, and New York inspectors, the branches at those points sent the following or similar telegrams to all consignees, on or about October 19:

Imperative you take up immediately all Elixir Sulfanilamide you may have dispensed. Product may be dangerous to life. Return all stocks our expense.

As a result of these telegrams large quantities of the "elixir" was returned to the manufacturer's establishments and there taken under local or federal control. But the extremely dangerous character of the drug necessitated the most searching check to guarantee, as far as humanly possible, its complete apprehension. Practically the entire field force of 239 Food and Drug Administration inspectors and chemists were assigned to the work. They had the wholehearted and effective coöperation of state and local food, drugs, and health authorities. As an additional aid, warnings by newspaper and radio were broadcast.

In spite of the manufacturer's telegrams many shipments were found still in dealers' hands. Innumerable prescriptions filled from these lots, as well as from shipments returned to the manufacturer, were found to have been only partly consumed by the patient and so were recovered.

EFFECTS OF THE DRUG

The victims of the "elixir" were ill from about seven to twenty-one days. They suffered intense pain. All exhibited very much the same symptoms: stoppage of urine, severe abdominal pain, nausea and vomiting; stupor; convulsions preceded death in some cases. Many persons who took the drug discontinued its use with the onset of unfavorable symptoms and recovered. One person took as much as seven and one-half fluidounces without ill effect. One child died from less than two fluidounces.

LIMITATIONS OF THE LAW

As indicated earlier in this report, the only basis of action under the Food and Drugs Act against the interstate distribution of the "elixir" was the allegation that the word implies an alcoholic solution, whereas the product was a diethylene glycol solution. The fact that the law contains no specific definition of "elixir" may be responsible for Doctor Massengill's statement in his letter to the American Medical Association, carried in the press of November 3: "I have violated no law."

Most drug manufacturers recognize a responsibility to the public far greater than that imposed by existing law. Some are known to have considered making a solution of sulfanilamide in diethylene glycol before the "elixir" was put on the market, but abandoned the idea on investigating the toxicity of the solvent. But the attitude of some drug makers is exemplified in Doctor Massengill's statement carried by the press on October 23:

My chemists and I deeply regret the fatal results, but there was no error in the manufacture of the product. We have been supplying legitimate professional demand and not once could have foreseen the unlooked-for results. I do not feel that there was any responsibility on our part. The chemical sulfanilamide had been approved for use and had been used in large quantities in other forms, and now its many bad effects are developing.

That evidence of possible danger from the internal administration of diethylene glycol was available prior to the marketing of the "elixir" is easily shown.

That a few simple tests on experimental animals would have demonstrated the lethal properties of the elixir is evident from the work reported by the American Medical Association. These results were confirmed independently by the Division of Pharmacology of the Food and Drug Administration in work yet unpublished.

While the "elixir" incident has been spectacular and has received much publicity, aside from the brevity of the period in which the killings occurred, it is but a repetition of what has frequently happened in the past in the marketing of such dangerous drugs as dinitrophenol, cinchophen, and other toxic substances.

It is worthy of note that, shocking as these instances have been, the actual toll in deaths and permanent injury from potent drugs is probably far less than that resulting from harmless nostrums offered for serious disease conditions. In these cases the harmful effect is an indirect one.

Sick people rely on false curative claims made for worthless concoctions, and thus permit their disease to progress unchecked. It may be too late when they lose confidence in the nostrum and seek rational treatment.

RECOMMENDATIONS FOR LEGISLATION

To protect the public from drugs which, like the "elixir," are dangerous because of their inherent toxicity, it is the Department's recommendation that legislation be enacted to provide at least the following:

1. License control of new drugs to insure that they will not be generally distributed until experimental and clinical tests have shown them to be safe for use. The definition of what constitutes a new drug should include (*a*) substances which have not been used sufficiently as drugs to become generally recognized as safe, (*b*) combinations of well-known drug substances where such combinations have not become generally recognized as safe, and (*c*) well-known drug substances and drug combinations bearing label directions for higher dosage or more frequent dosage or for longer duration of use than has become generally recognized as safe.

Exemption should be made for new drugs distributed to competent investigators for experimental work. A board of experts should be provided who will advise the Secretary of Agriculture on the safety of new drugs.

It is the Department's view that no other form of control will effectively safeguard the public from the dangers of premature distribution of new drugs. To increase the penalties for violations and to require label disclosure of ingredients would be helpful, but by no means fully adequate.

In the interest of safety, society has required that physicians be licensed to practice the healing art. Pharmacists are licensed to compound and dispense drugs. Electricians, plumbers, and steam engineers pursue their respective trades under license. But there is no such control to prevent incompetent drug manufacturers from marketing any kind of lethal potion.

2. Prohibition of drugs which are dangerous to health when administered in accordance with the manufacturer's directions for use. This would provide a more appropriate basis of action than that on which proceedings were instituted against the "elixir." A number of dangerous drugs are now on the market against which not even a trivial charge of violation can be made.

3. Requirement that drug labels bear appropriate directions for use and warnings against probable misuse. Much injury results from insufficient directions and from lack of warning against overdosage, or administration to children, or use in disease conditions where the drug is dangerous, or possibility of drug addiction.

4. Prohibition of secret remedies by requiring that labels disclose fully the composition of drugs. Many foreign countries now impose this requirement. Many drugs manufactured in the United States are exported to such countries under labels bearing such disclosure. The same drugs are sold to our citizens under labels that give no hint of their composition.

The physician, and the consumer who acts as physician to himself, both have a right to know what they administer.

Many poisoning cases result from choice of the wrong bottle from the home medicine cabinet, or from bottles left within the reach of small children. In such cases attending physicians are able to proceed intelligently and administer the proper antidotes or other treatment only if labels carry full disclosure of composition. Delays in obtaining this information by communicating with the manufacturer may often mean the difference between life and death.

Physicians are also handicapped in arriving at a correct diagnosis and beginning appropriate treatment when patients come to them after unsuccessful attempts at self-medication with secret remedies. The effect of such remedies may give rise to symptoms leading to erroneous diagnosis. But even if the diagnosis is correct, the kind of treatment to be used may depend upon what the patient has been taking. Again, in such circumstances, label declaration of composition may mean the difference between life and death.

The foregoing recommendations are limited to provisions which the Department believes should be enacted to safeguard the public from the dangers of drugs of one type. That type includes the inherently toxic drugs, such as the "elixir," dinitrophenol, and cinchophen. Many additional points should be considered if adequate protection is to be extended against even more widespread dangers to health and other abuses of public welfare arising from the inadequate control authorized by the present law over various other types of drugs.

PUBLIC HEALTH IS MAJOR EFFORT OF FEDERAL FOOD AND DRUG ADMINISTRATION*

Control of food and drug adulterations having a direct bearing on public health continued to require the major efforts of the Food and Drug Administration in the last fiscal year, according to the annual report of W. G. Campbell, Chief of the Administration.

Mobilization of an emergency force to follow the 1937 flood in the Ohio Valley and protect residents from food contaminated by flood waters was one of the conspicuous services by the Food and Drug Administration in the last year. Many of the forty-four federal food men assigned to the work had had experience in the 1936 flood. They were assisted by about eighty men from state and city food inspection organizations and from other federal agencies. The emergency organization functioned promptly. Work programs were under way in some areas before the flood waters began to recede. These crews handled food and drug preparations enough to have supplied a city of two hundred thousand population for a full year.

Another emergency requiring quick action by many field employees arose when it was discovered that emergency fumigation with hydrocyanic gas had made dangerous a quantity of raisins and other dried fruits—about 280,000 pounds—held up at the shipping point during the maritime strike and that these had been widely distributed. Food and Drug Administration workers quickly traced and seized nearly all the contaminated food, and the use of this method of fumigation for these commodities was immediately discontinued.

FINES VARY WIDELY

Mr. Campbell comments on the 1,700 court cases terminated in the year—1,355 food cases and 345 drug cases. "Fines varied," he says, "from sums as low as $1, $2, and $5 to a maximum actually paid of $1,500. Much higher fines were imposed in several cases, but were remitted in large part by the courts. Three jail sentences imposed in connection with second offenses were also suspended and the defendants placed on probation. In pleas of guilty to the adulteration of olive oil with tea-seed oil, two defendants were each fined $6,000, but $5,000 was subsequently remitted in each case.

"Courts in general vouchsafed no explanation for the imposition of nominal penalties. In one instance of a $2 penalty for the shipment of filthy and decomposed walnuts, the court indicated that it had taken into consideration the fact that the defendant had suffered a $1,400 loss in the seizure and destruction of the shipment by the Government. In another instance dealing with a practically worthless product offered as a treatment for serious diseases of the eye, the court imposed without comment, a fine of $1 and costs of $35."

"Other courts," Mr. Campbell continues, "have indicated a growing interest in the public protection afforded by the Food and Drugs Act. In passing sentence against a spinach canner who had entered a plea of guilty to the sale of dirty canned spinach, a court remarked that if the defendant was unable to manufacture clean food he had better get out of business and stay out of that court."

ISSUES IN LEGISLATION

Discussing possible changes in the law, Mr. Campbell says: "As in the three preceding years, legislative efforts have been continued in the Congress for a more adequate food and drug law. Senate Bill 5, introduced January 6, 1937, was passed by the Senate on March 9. This bill pro-

* From the United States Department of Agriculture.