ment produces a clear zone of inhibition 6 mm. wide.

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Establishment of the Drug Laboratory in the Bureau of Chemistry, United States Department of Agriculture*

By Lyman F. Kebler†

At various times, it has been suggested that the establishment and the early work of the Drug Laboratory of the Bureau of Chemistry of the U. S. Department of Agriculture ought to be written up and that I, being the only living person who is in possession of the necessary information, should write the story. This I have consistently hesitated to do heretofore for the simple reason that it necessarily brings me prominently into the picture. Of late I have, however, decided to put aside my personal feeling in the matter and write up the founding of this laboratory, including some of its early work, some of the prior activities of Congress and the lack of action on the part of Government officials in the field of pure and safe drugs for the suffering sick.

The first Congress of the United States in the second tariff act (1) included "Medicinal Drugs," among the imported articles to pay duty. Drugs used for dyeing were not included under this head. It also provided for the inspection and testing of all kinds of wines. The alcohol content was the chief factor to be considered. Determining the strength of alcohol was included in the first tariff act and all later general tariff acts. During the third session of the same Congress, an extensive tariff law was passed (2) containing 62 sections. Drugs as heretofore were included. A large proportion of the drugs in the early years of our country were imported. Cosmetics and perfumes were covered in the 1794 tariff act. General tariff laws were passed at irregular intervals by more than a score of Congresses. But, excepting the alcoholics, there was apparently a dearth of activity as to the character

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of drugs imported for about half a century. Yet we know from the published records of private investigators that adulterated, low grade and spurious drugs were coming into this country. This in time duly aroused both physicians and druggists. Opium was very commonly adulterated and of low grade, and opium, in those days and for many years later, was the physician's right hand. In time these rogueries were brought to the attention of Congress, and this resulted in the passage of the 1848 drug import law (3), which prohibited the importation of the above character of drugs. The law was administered by the Secretary of the Treasury. Politics seemed to have an early inning. The officials, it was alleged, seemed to be more interested in collecting revenue than in pure and safe drugs for the suffering sick. In spite of this, however, some very good work was done (4) under this law. It stimulated action along various lines, *e. g.*, the creation of standards and methods of analysis, which in turn called for better qualified examiners and better educational facilities.

The appropriation act of 1889 for the Department of Agriculture authorized the Secretary to investigate the adulteration of drugs. Succeeding Congresses granted the same authority to the Secretary over a period of years, but no action was taken, in the case of drugs, under this authority. In 1890, Senator George F. Edmunds' bill, prohibiting the importation of adulterated foods and drugs, became a law (5). Its enforcement was also vested in the Secretary of Agriculture. However, the drug portion was allowed to sleep, largely, I am informed, because Congress did not provide sufficient funds. In 1899 the Secretary of Agriculture was directed (6) to inspect, examine, test and, through the Secretary of the Treasury, refuse entry to any foods or drugs found adulterated and dangerous to health. The same authority was given in several later acts, but still the drug portion was allowed to remain dormant. Through all these years, there was marked agitation for a National Pure Food and Drug Law, and the Department figured prominently therein. So did the pharmacists. The drug interests therefore naturally became skeptical as to anything ever being done in behalf of pure drugs by the Secretary of Agriculture. But things took a turn for the better.

The 1901 appropriation act for the Department of Agriculture provided for raising the Division of Chemistry to the rank of a Bureau. The change was made July 1901. The chemist in his report for the fiscal year ending June 30, 1902, says in part: "The second line of work which the Bureau will undertake will be in the study of drugs. The work will be undertaken in hearty collaboration with the AMERICAN PHARMACEUTICAL ASSOCIATION, which already has a committee studying drug adulteration and the best methods of ascertaining them. The work will be divided into two portions: first, a study of the best methods of assaying drugs, and second, a study of the drug products bought on the open market, to determine their composition and the degree and extent of their adulteration. It is expected that the work will be fully inaugurated during the present year."

The Drug Laboratory was authorized about the same time (7). The first definite information received by the outside world, regarding the establishment of such a laboratory, was a letter of Dr. H. W. Wiley, sent to Professor John Uri Lloyd, on the letter head of the Bureau of Chemistry, June 16, 1902. It reads:

"We are about to undertake, under authority of Congress, a study of the composition and adulteration of drugs. We want to get a man of good training and some experience for the work. Could you suggest the names of some men who you think would render us faithful service and who are available? We can pay $2000 or $2500 per annum for a good, well-trained man. I would be glad to have suggestions from you in this matter.

Thanking you in advance for this courtesy, I am,

Faithfully,

H. W. WILEY, *Chief*"

In reply Professor Lloyd on July 16th, on letter head of the Lloyd Library, wrote Dr. Wiley as follows:

"My dear Professor Wiley:

"This morning I reach my desk after six weeks' vacation. Your letter is the first answered and I shall not delay for the stenographer. Lyman F. Kebler, Smith, Kline & French Co., Philadelphia, Pa., is the best man in America for your purpose in case he can be reached. His experience is exceptional in the line you wish an expert. His work is *unquestionable* as I know from experience of parallel investigations. He knows more to-day concerning tricks of the trade and probable adulterations than any man in the drug line and has ever aimed to enthusiastically attack adulteration and adulterators and mixers. If you can secure him you need have no time wasted in teaching or in wandering. He is expert in manipulation and conversant with the literature bearing on the subject of chemical examination.

"In my opinion he will be worth to you twice any other man and I hope his services may be secured. Should you desire details concerning Mr. Kebler's work I can furnish you data to substantiate the foregoing.

"Hoping this may reach you in time to serve you, and with regards, I am,

Sincerely yours,

JOHN URI LLOYD."

With the greatest of reluctance and for obvious reasons, Professor Lloyd's reply to Dr. Wiley's inquiry is included. It seemed to be the only course to follow. The commendations of a compatriot were of great service at the time they were given and very much appreciated, but they cannot profit me at my time of life. I am living on borrowed time.

The Secretary of Agriculture, in July 1902, requested the United States Civil Service Commission to hold an examination for securing eligibles for a chief of this laboratory. The Commission on August 16, 1902, issued the following announcement of the examination to secure eligibles for the position:

"CHIEF OF THE DRUG LABORATORY
BUREAU OF CHEMISTRY
DEPARTMENT OF AGRICULTURE
SEPTEMBER 15, 1902

"The United States Civil Service Commission announces that it is desired to establish an eligible register for the position of Chief of the Drug Laboratory, Bureau of Chemistry, Department of Agriculture. It will not be necessary for applicants to appear at any place for the examination.

"The examination will consist of the subjects mentioned below, which will be weighed as follows:

Subjects	Weights
1. Education and training	40
2. Postgraduate work and experience	40
3. (*a*) Thesis of not less than 1000 words, on the subject, 'To what therapeutic agents may State control at present be most advantageously applied.' (*b*) Scientific papers or reports of investigations published by the competitor	20
Total	100

"No one will be examined who is not a graduate in pharmacy or pharmaceutical chemistry (or an equivalent) and who has not since graduation had training and experience in the investigation of the purity and strength of substances used as therapeutic agents, and in the various sciences, a knowledge of which is essential to the successful conduct of such investigations. Experience in manufacturing pharmacy and a knowledge of commercial pharmacy will also be considered an advantage. Statements of degrees and college training must set forth the courses of study pursued and the time actually devoted to each. These statements must be certified by the appropriate officer of the school in which the work was done.

"Age limit, 20 years or over.

"From the eligibles resulting from this examination it is expected that certification will be made to the position of Chief of the Drug Laboratory, Bureau of Chemistry, Department of Agriculture, at a salary of $2000 per annum, and to other similar vacancies as they may occur.

"This examination is open to all citizens of the United States who comply with the requirements. Competitors will be rated without regard to any consideration other than the qualifications shown in their examination papers and eligibles will be certified strictly in accordance with the civil service law and rules.

"Persons who desire to compete should at once apply to the United States Civil Service Commission, Washington, D. C., for application Form 304, and special form, which should be properly executed and filed with the Commission, together with the required material, prior to the hour of closing business on September 15, 1902."

Form 304 is the application form used by the Commission for this type of examination. It is too long for even a partial inclusion in this write-up. It delves minutely into one's life history from the day of birth to the time of the examination; all kinds of work engaged in, why separated from the jobs, physical condition, chronic diseases, how freely one indulges in John Barleycorn, vouchers from two citizens as to character, use of profane language, intoxicating beverages, narcotics, etc. No one seems to know anything about the "special form" referred to, excepting that it possibly was a special form for this particular examination.

The Fiftieth Annual Meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION was held in Philadelphia, in September 1902. President H. W. Whelpley in his address called attention to the proposed investigation of drugs by the Bureau of Chemistry and that Dr. Wiley "has invited your president to outline what he considers should be the character and scope of this examination." In what manner the president complied with this request I have no knowledge but he did appoint (8) a "Committee to present the views of the AMERICAN PHARMACEUTICAL ASSOCIATION as to the most desirable character and scope of work of the new drug laboratory," consisting of A. E. Ebert, John Uri Lloyd and Lyman F. Kebler.

Professor E. L. Patch, in his report (9) as chairman of the Committee on Drug Adulteration, pointed out that the committee had received a communication from Dr. H. W. Wiley regarding the establishment of a pharmaceutical laboratory for studying the composition and adulteration of drugs. The report contains a number of recommendations and resolutions, which on motion were unanimously adopted. Two of the resolutions read: "(1) That the AMERICAN PHARMACEUTICAL ASSOCIATION offers to the Secretary of Agriculture its most cordial collaboration in this work, which promises so much benefit to the manufacturers of and dealers in drugs, as well as to the consumers thereof. (2) That this Association will use its influence with the Congress of the United States to secure a reasonable appropriation to properly carry on this work in a systematic and effective manner."

Dr. H. W. Wiley, at the first session of the Scientific Section, on invitation addressed its members (10) on the establishment of a Drug Laboratory in the Bureau of Chemistry. He outlined the nature of the work as he saw it to some extent. Said he: "Some people have the idea that the establishment of such a work as this by the Government will work a hardship on the druggist—the retailer, the wholesaler and the manufacturer. I do not think that the men in Congress who enacted this law had any such intention, and I can assure you the Secretary

of Agriculture has no such intention. On the contrary, the purpose is to help and aid, and not to annoy or embarrass. Some people have asked me, 'Do you think that Congress will continue these investigations, or will it let them drop in a little while?' Now, I have been in the public service for twenty years, and I have never yet known Congress to abandon a piece of work of this kind until it was finished, or until the end sought was attained. Congress having started this laboratory and given it an appropriation, will continue it and support it liberally. The Secretary of Agriculture has no right to come among you and select a man for chief of the new drug laboratory—that right is in the hands of the Civil Service Commission. In a short time an examination will be held for those who are willing to apply for the position of chief of the drug laboratory in the Bureau of Chemistry in the Department of Agriculture."

After listening to Dr. Wiley's address, I decided to take the examination, the final date for which was September 15, 1902. There were twenty-seven applicants. Ten passed. The rule of the Commission in such cases is to certify the three receiving the highest rating to the officer having charge of the work. I happened to be among the three and received the appointment November 26, 1902, to take office January 1, 1903. I was informed that I had received the highest rating. Due to my intimate connection with the business of my employer at the time, he asked whether my severance with the company could not be delayed for a time. To this fair request Dr. Wiley readily agreed.

The new chief reported for duty early on the morning of March 2, 1903, and found Dr. Wiley on the lower floor of the Bureau of Chemistry weighing out rations for his noted "Poison Squad," then used to test out the effects of food preservatives on digestion and health. The first official act the new chief performed was taking the oath of office, something I had never done before and it was very solemn to me. After Dr. Wiley could see me, we had a conference on the work. With a sober face he told me that Congress had authorized the establishment of the laboratory and appropriated the salary but failed to provide a place where the work could be done. He awaited the newcomer's reaction to this situation. The new chief told him that he would find a niche where he could do the work. Dr. Wiley smilingly said: "We can give you a chair, part of a desk, with reagents, chemicals and apparatus." These were the quarters I occupied for a time and I was happy in my environment. While looking over the stock of chemicals to furnish my worktable I found some of my old adulterated and mislabeled chemicals and supplies. Some of the brands of chemicals marked C.P., that I knew from previous experience, were far from being chemically pure. These findings were reported to the "Big Chief" and he immediately put me in charge of examining future chemical supplies of the Bureau, which was no small task in itself. These are some of the things found: weighted cochineal; arsenic in C.P. zinc, glycerin, sulfuric, hydrochloric and nitric acids; C.P. ether not even of U. S. P. quality; corrosive sublimate bearing a calomel label; C.P. molybdic acid eighty per cent pure; chromic acid loaded with sodium sulfate; glacial acetic acid and alcohol and the caustic hydroxides below quality claimed on the labels; potassium iodide containing sulfates and iodates; C.P. potassium cyanide testing over 100 per cent pure proved to be sodium cyanide. All these chemicals had up to this time been used for investigational work and as reagents.

At the 1903 meeting of the Association of Official Agricultural Chemists, a committee on the Testing of Chemicals was appointed, of which the Drug Chief was made chairman. In the discussion of the report of this committee in 1904, Dr. Wiley said: "The matter of the purity of reagents has been brought home to this Association by this report in a more pointed way than ever before. How many of our chemists test the purity of their reagents? Every chemist should resolve before leaving this meeting that he will not make another analysis for any work which is to be reported without assuring himself . . . . that his chemicals are sufficiently pure." Dr. Wiley was greatly shocked when he was informed regarding the quality of the chemical supply in the Bureau.

As will be recalled, there was great activity regarding the enactment of a pure food and drug law and Dr. Wiley was one of its chief protagonists. His fort was foods. The Drug Chief was instructed to give senators and congressmen every possible information and assistance in the matter of pure and adulterated drugs. The United States Pharmacopœia and the National Formulary were embodied in a number of the bills introduced in the late nineties but for various reasons the Formulary was not included in later bills and the Pharmacopœia only retained. This was strenuously objected to by many drug interests, promoters of proprietaries in particular. The result was a struggle for a more inclusive definition for drugs in the National Law. Dissatisfied drug representatives appeared at a special hearing January 20, 1903. During this hearing (11), the Omnibus drug definition was born. This definition precipitated a marked discord in the pharmaceutical profession and made plenty of demands on the Drug Laboratory, some of which are referred to in the Department of Agriculture annual reports and need not be discussed here. It should be noted here, however, that the Drug Laboratory called attention to the desirability of including the National Formulary, as a standard, in a National Food and Drug Law. Dr. Wiley was in full accord with this idea, and it was included in later Congressional bills and finally recognized in the National Law of June 30, 1906.

One day the "Big Chief" called me into his office and said: "The Bureau of Printing and Engraving has submitted a number of samples of glue and I would like to have you test them." The Drug

Chief told him that he had never tested glue and did not know anything about the subject. In reply the Boss said: "You know as much about testing glue as anyone in the Bureau." I further protested that glue was not a drug. He retorted: "Glue is certainly a drug around here and it is your job." He had shopped, without success, around the Bureau for someone to do the work and the Drug Chief was a newcomer and the logical victim. He took advantage of the definition, "A drug on the market," in this case meaning the Bureau. Some of my fellow chemists considered it a good joke. I tested the glue and did not find it such a difficult task—nothing compared with some of the knotty drug adulterations I had been called on to unravel in former years.

The glue testing represented collaboration with other branches of the Government, for which Dr. Wiley was an enthusiast. A few months later he again called me into his office, handed me a number of drug samples called "Vitality Pills," submitted by the Postmaster General for examination and report as to whether the claims made therefor were warranted. They were alleged, among other things, to contain animal extract derived from healthy bulls. Here was something novel and weird. We discussed it *pro* and *con* on numerous occasions. An examination, however, showed that these pills were of the same general composition as the commonly so-called listed aphrodisiac pills. We discussed the subject with several outstanding physicians and reached the conclusion that the claims were far-reaching and many wide of the truth and so reported to the Postmaster General. Here another thing happened. The Secretary of Agriculture did not want to sign this kind of a report. It then fell to Dr. Wiley's lot to sign and get the reports into the Solicitor's hands, which was done. The promoter was cited for a hearing, alleging the fraudulent use of the mails. After the hearing a fraud order was issued, debarring the promoter from the use of the mails, which was a signal for a royal legal battle, such as I had never seen before, but have been in many since. The case was vigorously contested, but the Government won, which meant that we would be required to do more work for the Post Office Department, in the matter of the fraudulent use of the mails. Poisons in the mails came next into the picture.

In 1903 the Drug Chief was appointed a referee on "Medicinal Plants and Drugs," in the Association of Official Agricultural Chemists. Under this appointment the methods for estimating morphine in opium were taken up and reported on for several succeeding years.

Due to the untruthful advertising and adverse publicity given proprietary medicines, either directly or indirectly, as the result of the information brought out in connection with the hearings under the various food and drug bills and otherwise, the Council on Pharmacy and Chemistry, of the American Medical Association, was organized in 1905. Dr. Wiley and I were charter members, and took a part in the work for a number of years. The Drug Laboratory made quite a few analyses of a number of proprietaries published by the Council (12), among them the acetanilid mixtures.

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Book Reviews

Organic Syntheses. An Annual Publication of Satisfactory Methods for the Preparation of Organic Chemicals. Volume XX. CHARLES F. H. ALLEN, Editor-in-Chief. v + 113 pages. John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y., 1940. Price, $1.75.

This, the twentieth volume of this series, is similar in arrangement of its contents to that of preceding volumes. It contains directions for the preparation of 39 compounds involving many types of reactions. In addition, there are included for each preparation equations indicating the chemical changes involved, a detailed statement of the procedure to be followed, notes on points to which particular attention should be directed, a statement, with references, covering other methods of preparation, and illustrations of apparatus. The book is a useful reference work for anyone engaged in the preparation of organic compounds.—A. G. D.

Physical Constants of Hydrocarbons. Volume II. *Cyclanes, Cyclenes, Cyclynes, and Other Alicyclic Hydrocarbons,* by GUSTAV EGLOFF. 605 pages. Reinhold Publishing Corp., 330 West 42nd St., New York, N. Y., 1940. Price $12.00.

This book is the second volume of a four-volume work giving values for the boiling point, melting point, density and refractive index of pure hydro-