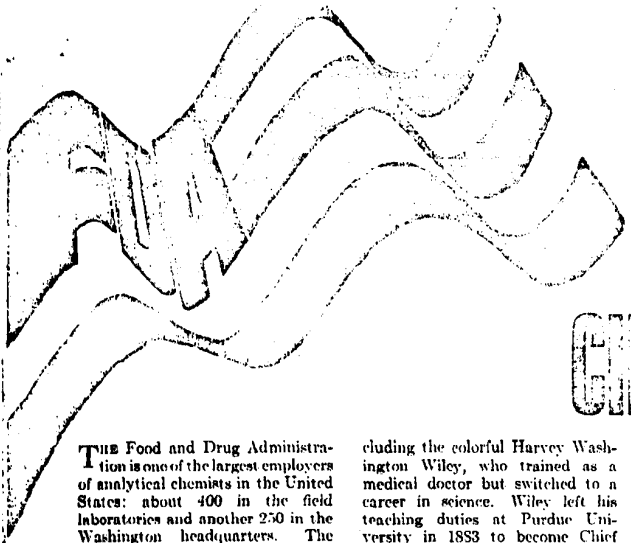

CHEMISTRY

THE Food and Drug Administration is one of the largest employers of analytical chemists in the United States: about 400 in the field laboratories and another 250 in the Washington headquarters. The agency has moved a long way from the days when the chief laboratory instruments were the analytical balance and the microscope, and the prime analytical challenge was the detection of tenseed oil in olive oil. The changes reflect not only the development of analytical science but also the transformation in modern life.

Evolution of an Agency

In the last quarter of the 19th century, the United States underwent a transition from a rural to an urban society, and millions of citizens who formerly produced their own foods, medicines, and other consumer products now had to depend on commercially processed products. Although the majority of commercial producers were legitimate, others were not. It was not unknown for a food processor to make canned peas greener by adding copper sulfate, to preserve foods with formaldehyde, borax, or sodium benzoate, or to defraud the consumer by adulterating expensive natural products with cheap substitutes. The market abounded in quack drugs whose popularity owed much to their considerable alcohol content.

In time public concern became aroused, and a number of scientists began to attack the problem, including the colorful Harvey Washington Wiley, who trained as a medical doctor but switched to a career in science. Wiley left his teaching duties at Purdue University in 1883 to become Chief Chemist of the U.S. Department of Agriculture. Starting with two or three chemists whose primary duty was to analyze fertilizers, Wiley soon expanded his activities to include studies of food adulteration. At first he considered the main threat to be to the consumer's pocketbook instead of his health. But as public opinion began to solidify in favor of a national food and drug law, Wiley knew that to justify legislation, it would be essential to establish the degree of health hazard. Around the turn of the century, he formed his famous "Poison Squad," a group of healthy young men who, under his direction, limited their food intake to a closely supervised diet to which known quantities of preservatives and adulterants had been added. Their urine and feces were collected and examined, and a close check was kept on their state of health. It was a rough test by today's scientific standards, but although results were not entirely conclusive, it became evident that such preservatives in foods were indeed harmful to human health.

After a long and often discouraging struggle in which he was opposed by many pressure groups, Harvey Wiley finally saw the Food and Drug Act of 1906 passed by both Houses of Congress and signed into law. He then found that the hardest part of the fight was just beginning: that enforcement of the law was to be even more difficult than its enactment. But as the opponents of food and drug regulation continued their opposition to regulation, he and his various successors through the years maintained a record of equally vigorous enforcement.

Originally, enforcement activities were lodged in the USDA Bureau of Chemistry, but in 1927 the Food and Drug Administration was established as a separate entity within USDA. After passage of the 1938 *Food, Drug and Cosmetic Act*, containing such innovations as premarket testing of new drugs, FDA was removed from USDA and placed under the Federal Security Agency, which became the nucleus of the Department of Health, Education, and Welfare established in 1953. The basic structure remained much the same until 1961 when the first of several major reorganizations was announced. The present structure appears in Figure 1.

For many years FDA was a small agency with a tight budget. As recently as 1955, a staff of 800 with a budget of only $5.1 million was responsible for regulating goods with an annual value of $63 billion. After a survey and report by a Citizens' Advisory Committee in 1955, FDA was instructed to quadruple its resources to carry out its responsibilities more effectively. The picture for fiscal year 1972 was considerably different from that of 1955. FDA's budget was $110

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Since the establishment of the Food and Drug Administration, the problems to be solved and the tools to solve them have increased several orders of magnitude. At the same time, acceptable levels of sensitivity in measurements have decreased from the milligram to the nanogram or picogram level

FOR CONSUMERS

million, and the agency had more than 4000 employees, although these amounts are still short of those needed to attain FDA's goals (*1*).

FDA Today

Resources for FDA's regulatory work must be spread over a wide area of domestic and imported products. In addition to the basic FD&C Act, the Import Milk Act, the Filled Milk Act, and the Tea Importation Act, FDA is responsible for enforcing the Food Additives and Color Additives Amendments, the Kefauver-Harris Drug Amendments, the Fair Packaging and Labeling Act, the Hazardous Substances Act and its amendments (Child Protection and Toy Safety Acts and Poison Prevention Packaging Act), and portions of the Public Health Service Act including the Radiation Control for Health and Safety Act. Besides its other regulatory work, the agency must test and certify every batch of color additives, antibiotics, and insulin drugs manufactured in the U.S. The retail value of all products under FDA jurisdiction is now over $230 billion, representing almost 38 cents of every dollar spent by consumers. The current annual cost of FDA protection of consumers is about 53 cents per person.

In contrast to many organizations, FDA's main arena of action is in the field. Many of the episodes that catapult FDA into the news begin at one of the 19 district offices located in major cities throughout the U.S. An inspector is sent to check a complaint received at the district level, or he sees the first indications of trouble in a routine establishment inspection. He obtains samples (usually by purchase) and sends them to the district office for laboratory examination by chemists or microbiologists. If the results warrant, the investigation then expands, sometimes to a full-scale program. If an imminent hazard to health is involved, several districts may cooperate in round-the-clock work until the problem has been brought under control.

FDA may take action against a violation in one of several ways: by court-ordered seizure of the product, injunction, or criminal prosecution in a court of law. Each type of action must, of course, be based on sound evidence, and those who are accused of violation are protected by due process. The most serious type of action is the criminal court case; it is also the most expensive in terms of money, manpower, and time. Seizure is carried out by the district through the Federal courts, but the decision to prosecute must be made at headquarters in Washington.

Since its earliest days, FDA has depended heavily on laboratory analyses. An analytical result can be no better than the method used to obtain it, and the search for better methods is unrelenting. Even under the most severe regulatory pressures, some time has always been reserved for methods development. A regulatory method need not be elegant, but it must have certain other characteristics: It must be accurate, precise, reliable, specific, sensitive within the range of interest, and practical. Preferably, it will be rapid and inexpensive, but these are secondary considerations. Most important, it must be capable of giving the type of results that can be used successfully in court. The scientific wit-

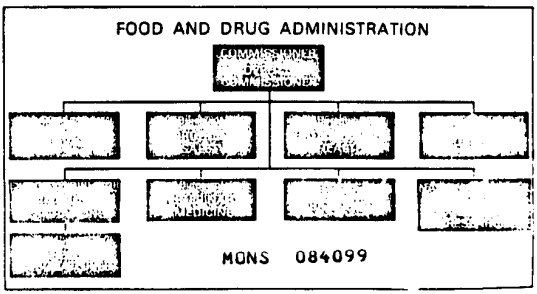


Figure 1. Organization of Food and Drug Administration (July 1972)

Figure 2. Chemists at Kansas City District examine food samples for pesticide residues by gas chromatography

ness for FDA must be able to defend his testimony against cross-examination by a defense attorney. The defense may bring in other scientific experts who testify that they obtained different results by a different method. For these reasons, FDA prefers to use standardized, validated methods such as those of the United States Pharmacopeia (*2*) or the National Formulary (*3*) for drugs and the Association of Official Analytical Chemists (AOAC) for foods and other commodities (*4*). "One-man methods" are open to attack and must be strongly supported by validation.

FDA has been quick to adopt modern techniques and instruments as they are developed and to exploit them for the agency's unique mission. The early reliance on color tests, volumetric and gravimetric analyses, and microscopic identifications has undergone complete metamorphosis. FDA now utilizes a range of techniques including infrared, visible, and ultraviolet spectrophotometry; nuclear magnetic resonance, atomic absorption, electron spin resonance, and mass spectrometry; gas-liquid, thin-layer, liquid-liquid, partition, ion-exchange, and absorption chromatography; X-ray diffraction, fluorescence, electron microscopy, and polarography, among others (Figure 2).

Mycotoxins

Problems of regulating consumer products are rarely single incidents that can be solved simply and quickly. Even the recent death from contaminated vichyssoise soup was only one tragic episode in the continuous fight against toxic organisms such as *Clostridium botulinum*. Many of FDA's most serious problems arise from natural contaminants. Modern analytical techniques permit FDA to detect many chemical contaminants that previously escaped detection. An example is the mycotoxins, of which the aflatoxins are best known.

The aflatoxins are a group of toxic metabolites formed chiefly from the mold *Aspergillus flavus*, which occurs naturally on groundnuts and other crops. Aflatoxins have probably infested crops since the beginning of agriculture but were not recognized as a health hazard until the early 1960's, when an outbreak of "Turkey X" disease in England was traced to animal feed containing peanut meal from moldy peanuts (*5*). The research laboratories in Washington undertook an extensive research program on all phases of the mycotoxins, including their nature, effects, formation, natural occurrence, and assay. Techniques were developed for the isolation and purification of the mycotoxins for chemical characterization and identification (*6*). A single nut was labeled radioactively to check the homogeneity of a groundnut composite (*7*). Physicochemical procedures were based on fluorescence and thin-layer chromatography and bioassays first on ducklings as test animals and then more successfully on teratological effects in the chicken embryo (*8*). Continuing research has disclosed a new mycotoxin, named aspertoxin, which has been isolated and its structure elucidated (*9*).

Specially trained district laboratory analysts determine aflatoxins in import and domestic samples. The New Orleans District has been designated as a specialized laboratory for the analysis of mycotoxins in FDA surveys of various classes of foods to establish their potential for mycotoxin contamination. The sensitivity of the aflatoxin chemical assays is now well below 20 ppb. Methodology has been extended to a number of commodities and to large-scale samples, in which a direct extraction of water-wetted samples with chloroform is combined with a silica gel column for defatting and cleanup (*10*). This procedure provides enough material for chemical confirmation, for example, by formation of derivatives with thionyl chloride and formic or acetic acid (*11*).

Mercury in Foods

Heavy metals in foods—lead, arsenic, mercury, cadmium—have plagued mankind for generations, and as one source of contamination is brought under control, another seems to take its place. Mercury in fruits and vegetables as a result of agricultural practices was a source of hazard during the early 1930's, but the development and acceptance of the "safe" organic pesticides were thought to solve the problem. But by 1952 mercury had again become a matter for concern because of its use as a fungicide to treat seed wheat. Industrial use of mercury, chiefly in chlor-alkali plants, has now generated a greater hazard: The mercury enters aquatic systems and is transferred to the food chain through fish in the form of highly toxic methyl mercury.

In late 1969 a family living near Almagordo, N.M., was poisoned after eating meat from slaughtered hogs which had been fed mercury-treated seed grain (*12*). A colorimetric method was already available to determine the mercury content of the grain (*13*); although lengthy, it had been collaboratively studied by the AOAC and was suitable for the relatively small numbers of grain samples that FDA

normally checked during a year. The grain sample is digested with HNO_3 and H_2SO_4 under reflux in a special apparatus, interfering metals are removed, and mercury is isolated by dithizone extraction and then determined by photometric measurement of mercury dithizonate. By this method, analysis of the grain fed to the hogs showed 32 ppm mercury (*12*). The method proved to be unsuitable, however, when the need arose to determine mercury in fish.

Japanese families suffered poisoning from eating fish contaminated with mercury in a number of episodes during the 1950's in the area of Minamata Bay and again in 1964–65 (*14*) at Niigata. As early as 1964, Sweden became concerned about the contamination of its food supply with mercury arising from the use of mercurial fungicides in agriculture and mercurial slimicides in paper mills. In 1968 the Swedish delegate to the Codex Committee on Food Additives reported that mercury levels in fish had become a matter of real concern.

In early 1970 Canadian authorities became alarmed at the degree of mercury pollution in certain Canadian lakes and rivers, owing chiefly to chlor-alkali chemical plants, and they closed them to commercial fishing. The FDA districts at Detroit, Minneapolis, Cincinnati, and Buffalo began an immediate investigation of the Great Lakes area. Chlor-alkali plants were visited, and agricultural runoff and other industrial sources of pollution were checked. Samples of fish from suspected waters were collected and analyzed. Data on mercury in fish were reported from a number of sources, many of them outside FDA, and none of the sources used the same analytical procedure. There was no means of judging the accuracy and reliability of the data. To provide reliable data on which to make a sound regulatory decision, it was necessary to have a rapid, accurate, precise, sensitive analytical method which could be collaboratively studied and adopted as official by the AOAC. The Denver District, which had already begun method studies, was asked to institute a crash program to develop such a method. The final procedure utilizes measurement of the volatilized mercury vapor by flameless atomic absorption (*15*). The fish muscle is digested with concentrated acids; the mercury is reduced with stannous chloride–hydroxylamine and then volatilized at room temperature in a stream of air (Figure 3). The air is pumped through a gas cell where the mercury vapor is measured by atomic absorption at 253.7 nm. As little as 0.05 ppm total mercury in the edible portion of the fish can be determined. Scientists of the Washington laboratories confirmed these results by neutron activation analysis (*16*). The method was collaboratively studied by nine laboratories, adopted as official by the AOAC, and used for rapid examination of large numbers of fish samples by the field districts and other laboratories (*17*).

Figure 3. Digestion of fish sample for determination of mercury

However, this method determined only total mercury, whereas methyl mercury was the actual toxic factor. Dr. Gunnell Westöö of the National Institute of Public Health at Stockholm, who had developed a gas chromatographic method for methyl mercury in several foodstuffs (sensitivity of 0.01 ppm), visited FDA, and her method (*18*) was studied at the headquarters' laboratories. Some modifications were made in the procedure, and checks were run between the total mercury and the methyl mercury content of fish. From these and other results, practically all of the mercury in the fish was present as methyl mercury (*19*). Thus, the method for total mercury was adequate for FDA's regulatory work on fish.

Pesticides and Mobile Laboratory

By the mid-1950's, FDA was deeply involved in analysis of raw agricultural products for residues of the new organic pesticides developed after World War II. Most of the original procedures were long, tedious methods based on classical chemical reactions aimed at detecting residues of a single pesticide. Later, screening methods involving paper and thin-layer chromatography and finally gas-liquid chromatography were used to examine a sample for a large number of residues simultaneously (*20*).

Time has always been critical in FDA work. Examination of raw agricultural products, however, posed an even greater time constraint. The FDA inspector would sample a lot of a given raw vegetable at some remote point, usually near the harvest area, and then have to ship the samples by airmail or freight to the district laboratory. If the product did contain excessive pesticide residues, valuable time was lost.

To speed pesticide residue analysis, in 1961 FDA first experimented with mobile laboratories. Standard small house trailers were converted to laboratories by installing appropriate furniture and equipment. The only instruments were sample preparation equipment, a simple

visible spectrophotometer, and paper and thin-layer chromatographic equipment. These trailer labs were not self-contained; they required sewer facilities and hookups for electricity and water. In practice the trailer was transported to some central location near a major growing area during the harvest season and operated as an examining laboratory for samples collected from the immediate vicinity.

These early trailer laboratories did yeoman work in field examination of products for pesticide residues and also as examining stations for physical or sensory analysis of products offered for import into the U.S. through remote border stations. It was soon evident, however, that they were not adequate for the complex analytical examinations that needed to be made in the field.

In 1964 FDA accepted delivery of brand-new, large custom-built trailer laboratories, nearly 40 ft long and outfitted with the equipment needed to perform most chemical analyses in the field. The new labs contained full operating hood space and a gas-liquid chromatograph equipped with electron capture detector for simultaneously screening raw agricultural products for a large number of pesticides at extremely low residue levels. They still required utility and water hookups and had to be transported from one location to another.

These new trailers proved to be the key to rapid identification of potential pesticide residue problems. During 1967, for example, the trailer laboratory operating out of the FDA Dallas District office was stationed at Laredo, Tex. Cantaloupes being imported from Mexico contained residues of the pesticide chemical, endrin. Although use of endrin is not permitted on most foods, it is sometimes found in the soil from previous application on nonfood crops such as cotton. Many vine and root crops leach the endrin from the soil during growth. Cantaloupes are a major export item for Mexico, and the Mexican government became concerned when the problem arose. Meetings were held between representatives of the Mexican government (arranged through the U.S. Department of State), U.S. Customs, FDA, and U.S. and Mexican importers and growers. A crash program was instituted to examine all shipments of Mexican cantaloupes, in which the trailer laboratory at Laredo played a key role. During a 6-week period a total of 1200 samples was examined by the Dallas, Denver, and New Orleans laboratories of FDA and the trailer laboratory at Laredo. As a result of the examinations, 106 railcars of cantaloupes were detained and destroyed.

Besides performing large numbers of analyses, the trailer laboratories have helped identify some interesting new analytical problems. In 1971 the trailer operating out of FDA's Los Angeles District at Nogales, Ariz., routinely examined a sample of Chinese peas imported from Mexico and found an unidentified pesticide residue. Further investigation showed that this residue was a halogenated organophosphate. By use of a variety of instrumental techniques at the district laboratory, the residue was finally identified as a pesticide not registered for use in the United States. It apparently had been used provisionally or experimentally in Mexico prior to its legal use in the United States and was later granted a temporary registration.

The FDA New York District is responsible for one of the largest ports in the world. In 1971 the District converted van-type delivery trucks into self-propelled mobile laboratories to be used directly on the docks to expedite examination of import goods offered for entry into the U.S. (Figures 4a,b). Although these vans could be used only for physical or sensory tests and some minor chemical determina-

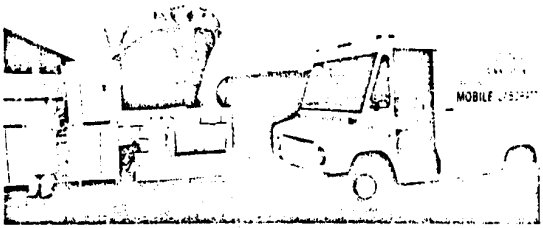


Figure 4a. New York District's mobile laboratory at docks for examination of imports

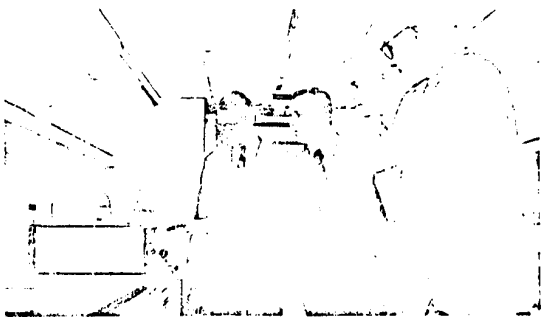


Figure 4b. Inside one of FDA's new mobile laboratories. Richard Klug of FDA points out special features to (left to right) HEW Secretary, Elliot L. Richardson; Assistant Secretary for Health and Scientific Affairs, Merlin K. DuVal; and FDA Commissioner, Charles C. Edwards

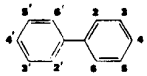
tions, they were the first truly mobile FDA laboratories. They could be driven into a warehouse or alongside a ship at berth or parked at any convenient spot near the goods being sampled.

This experiment was so successful that FDA has just purchased new mobile laboratories—custom-built, self-propelled laboratory vans, each equipped with a 5000-watt gas-powered generator and pressurized water and sewage collecting systems. They have multichannel mobile telephones for quick communication with the district office. Present plans call for these mobile laboratories to be used for examination of import samples at major ports in the same way that the New York District uses the converted vans.

PCB Problem

During the fall of 1968, Japanese investigators (*21*) reported the outbreak of a peculiar disease which resulted from eating rice oil contaminated with Kanechlor, a mixture of polychlorinated biphenyls (PCB). In 1971 USDA and FDA, in a cooperative investigation, found that fish meal, poultry, and eggs had become contaminated from industrial accidents in which a PCB mixture leaked from heat-exchange equipment into the food product. Thousands of hens and broilers were voluntarily destroyed, and adulterated eggs were seized. PCB's have also migrated into foods from packaging and other sources. FDA proposed regulations to control the accidental contamination of foods and to limit PCB residues from environmental or industrial sources (*22*).

These industrial chemicals, of which there are 210 theoretically possible isomers, are used extensively in electrical insulation, heat-exchange liquids, inks, paints, and plastics. Chlorine may be substituted in one or more of the numbered positions of the biphenyl molecule.



They are commercially produced by chlorination of the parent biphenyl nucleus to certain specified chlorine contents, producing a mixture of isomers with properties similar to those of DDT and its analogs. Hence, any PCB's in a food product will be carried through a typical pesticide determination and may interfere with the interpretation of the gas chromatogram.

Because of this and because of alterations in isomeric composition of the PCB mixture through weathering, metabolism, adsorption, and solubility effects, a fully satisfactory analytical method poses many problems. A procedure has been developed by FDA chemists and used to separate PCB's from chlorinated pesticides by selective elution from a silicic acid column (*23*). Work is continuing to improve the method, since recovery decreases with decreasing chlorine content so that separation of the mono-, di-, and triisomers from DDT and its analogs is not always complete (*24*).

Drugs and FDA

Although FDA spends 39% of its funds on foods, it allocates nearly as much—36%—to drugs. In addition to pharmacology, toxicology, and bioavailability studies, methods are continually being developed to test the safety, purity, potency, and effectiveness of drugs for both human and veterinary use. Until a few years ago, these methods were designed chiefly for use on composites, for instance, a sample of 20 tablets. Recent research, however, has shown that the quantity of active ingredient may vary greatly from tablet to tablet or capsule to capsule. These drugs are used in small amounts in a tablet or capsule in conjunction with a relatively large amount of filler or binder, and even slight deviations from the labeled amount of active ingredient may markedly change the potency of the drug, presenting a possible hazard to the patient. The trend now is toward individual tablet analysis (ITA), which may require 10, 20, or even more analyses of single tablets in place of duplicate determinations of a 20-tablet composite. Because of the tremendous workload involved in conventional analysis at this level, FDA turned to automated analyses. In addition to automatic analyzers in the field districts, the agency has set up the National Center for Drug Analysis at

St. Louis; this installation operates on an assembly-line basis, relying mainly on automated and semiautomated procedures and on calculation of data by computers and programmable calculators. The Center's research unit adapts established methods to automated operation and develops new procedures as the need arises (*85*).

One of FDA's most interesting research studies was the identification of Krebiozen. Introduced in 1950 as an agent for the treatment of cancer, Krebiozen was said by its producers to be a biological product derived from the serum of inoculated horses. In 1962 after passage of the Kefauver-Harris Drug Amendments, its sponsors filed an Investigational New Drug Application. When FDA began its investigation, requests for a sample of Krebiozen substance for examination were ignored by the manufactures. After several months, they did provide an FDA inspector with a single ampul containing a small quantity of material which they said was Krebiozen substance. The same sponsors had submitted Krebiozen samples to the National Cancer Institute two years earlier, and an infrared spectrum of those samples was available. The melting point, empirical formula, and molecular weight of the substance had been provided by the manufacturer.

The infrared spectrum suggested the possibility that the substance might be an amino acid, and since it was somehow associated with horse blood, FDA scientists proceeded on the hypothesis that it might be a known amino acid present in blood. By examining authentic spectra of amino acids, it was discovered that the Krebiozen spectrum was identical with the published spectrum of creatine monohydrate, a well-known, readily available amino acid which is present in blood.

To prove that the substance given to FDA was the same as the National Cancer Institute material and therefore was creatine monohydrate, FDA scientists in conjunction with members of university faculties examined the sample by X-ray diffraction, mass spectrometry, microscopic crystallography, thin-layer and paper chromatography, and melting point, in addition to infrared spectrophotometry. The problem was especially difficult because of the minute amount of material available for analysis. All of the tests confirmed the identity of the substance as creatine monohydrate, and none of them revealed more than a trace of any other substance.

This led immediately to another question. The vehicle in which the injection form was dissolved was mineral oil; yet, creatine monohydrate is not soluble in mineral oil, even in low amounts. Then, what was the substance in the mineral oil? FDA scientists extracted the mineral oil injections with water and water–ethanol mixtures, evaporated the aqueous fraction, and separated it chromatographically. Traces of creatinine were detected, as well as larger amounts of a chemically similar substance which was judged probably to be 1-methylhydantoin. Creatine will hydrolyze first to creatinine and then to 1-methylhydantoin upon heating with amyl alcohol and small quantities of alkali. During the evaporation of the aqueous fraction of the extract, an odor like that of amyl alcohol had been detected, and glc had shown that *n*-amyl alcohol was present in samples of the mineral oil injection in a concentration that correlated with that of 1-methylhydantoin.

To duplicate the means by which creatine had been incorporated in the mineral oil, FDA scientists dissolved creatine in amyl alcohol at the proper concentration; to 50 ml of this solution was added a pellet of KOH, and the solution was refluxed. The reflux was sampled at intervals, and the sample checked by tlc. After 30 min, all the creatine had hydrolyzed to creatinine plus a trace of 1-methylhydantoin; by 24 hr, the material remaining was virtually all 1-methylhydantoin. Upon analysis, 1 ml of this end product behaved exactly like the product furnished by the manufacturer. Tlc showed that samples of the original product contained small traces of creatinine plus 1-methylhydantoin; for further identification, 1-methylhydantoin was isolated from the oil by paper chromatography, recovered from the paper, and incorporated in a micro KBr disk. The infrared spectrum was identical with that of pure 1-methylhydantoin

under the same conditions. In this manner, it was demonstrated that the substance alleged to be a new drug, Krebiozen, was actually creatine monohydrate and that some samples of Krebiozen injection contained 1-methylhydantoin, a derivative of creatine.

Keeping Current

As with all scientists, the possibility of technical obsolescence of FDA's analytical chemists must always be considered. To combat obsolescence, several tactics have been devised. FDA scientists are encouraged to be active in professional societies, to take part in scientific meetings and seminars, and to continue their education, often at the agency's expense. Because the standard curricula do not always meet FDA's needs, the agency joined with Georgetown University, Washington, D.C., in 1964 to set up the "FDA Institute for Advanced Analytical Chemistry" (*36*). The University provided three laboratories for the exclusive use of the course plus full-time and part-time faculty members. Some of the analytical instrumentation (mass spectrometer, computer) was furnished by the University, and an additional $222,000 worth of instrumentation was provided by FDA, including gas chromatographs, atomic absorption equipment, all types of spectrophotometers, nuclear magnetic resonance equipment with a time-averaging computer, and polarographs. The curriculum consisted of a 12-week intensive course of advanced theory and application of instrumental methods to analytical chemistry, comprising 91 hr of lecture, 62 hr of recitation, and 204 hr of laboratory work. The University gave each student an academic grade according to its usual criteria and awarded graduate credit at its own discretion. Several positions in each course were reserved for scientists from other government agencies, industry, the academic world, and foreign countries. By April 1969 the majority of FDA's analytical chemists had completed the course, and the Institute changed its program to special courses of one, two, or three weeks on such topics as liquid chromatography, use of computers in the analytical laboratory, frontiers in analytical techniques and photochemistry, and fluorescence and phosphorescence spectroscopy.

In May 1966 a Science Advisor Program was initiated for the benefit of the field districts. In this program a professor of chemistry or microbiology (or both) on the faculty of a university within easy commuting distance of the district is employed as a consultant and advisor to the laboratory staff and management of the district (Figure 5). Selection of advisors is based on activity in both teaching and research at the university and on direction of graduate study in an area in which analytical chemistry or analytical microbiology is a principal part of the investigation.

Since passage of the 1906 Food and Drug Act, both the problems to be solved and the means for solving them have advanced by several

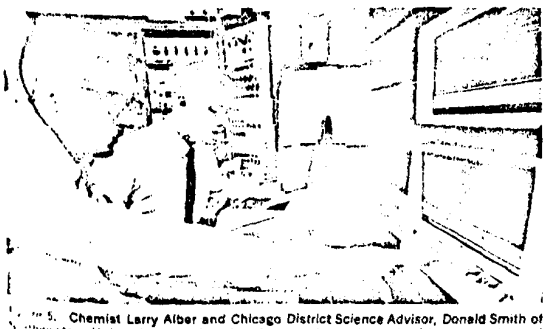


Figure 5. Chemist Larry Alber and Chicago District Science Advisor, Donald Smith of Northwestern University, have interfaced a gas chromatograph with a computer and developed a program for on-line computation of analytical data

orders of magnitude, in the same way that the acceptable level of sensitivity has dropped from the **milligram** to the **nanogram** or **picogram** level. For effective protection of the consumer, FDA must continue to use every possible resource, including more adequate budgets, better qualified personnel, more advanced instruments, and newer techniques. But one of its chief tools will continue to be analytical chemistry.

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