SEPTEMBER 1970

FDA PAPERS

Why FDA Analyses Stick
AOAC Helps Assure Validity

"We are carefully to preserve that life which the Author of nature has given us, for it was no idle gift."

Harvey W. Wiley, 1844-1930
Father of the Federal Food and Drugs Act of 1906

From his commencement address "Life and the Coming Time" Hanover College, 1867

Although the present degree of concern over chemical contamination of the human environment has been with us only a few years, chemical contamination of one part of the environment, the food we eat, has been one of FDA's major concerns for a great many years. During these years FDA, under general and specific statutes, has developed efficient regulatory and scientific methods for protection of the consumer from toxic chemicals in or on his food.

But this methodology has involved mainly those foods that might be reasonably expected to become contaminated under given conditions. Thus these methods have involved such chemicals as pesticides used in producing, processing, and storing foods; drugs used in food-producing animals; and direct or indirect food additives.

Little attention has been given to other ways that toxic chemicals used chiefly in industrial processes may find their way into food through contamination of the earth, bodies of water, and the atmosphere, when considered in context with the ecological patterns of plant and animal life that may tend to concentrate these chemicals in hitherto unsuspected food sources (see page 8).

More study is needed on the kinds of industrial chemicals that pose a threat to human health when loosed in the environment; the nature and extent of the threat; the legal, regulatory, and educational safeguards needed to protect the public health; and the scientific methods needed to detect, identify, and measure these chemicals in foods.

quotes

"In one instance, in the objections filed to our implementation of the NAS-NRC recommendations, there was submitted a list of more than 100 so called scientific studies and reports purporting to show something regarding a particular drug. It took considerable time for our legal and scientific staffs to establish that this evidence was mostly irrelevant and obviously inadequate.

"Such a submission does a disservice to the Food and Drug Administration (even if we prevail), to you who are upholding professional standards, and to the public for whom we should all be spending our time more productively, and finally to the drug industry."

John Jenninet, M.D., Assistant to the Commissioner for Medical Affairs, at the 93rd Annual Meeting of the American Bar Association, St. Louis, Missouri, August 12, 1970.

"The GRAS list has been the point of focus for concerns over food safety. The cyclamate incident of last October heightened this concern. In its wake, the President directed the Agency to review the entire list to be assured that consumer safety is being adequately protected. There will, no doubt, be a harder look at these food additives. There will, no doubt, be some deletions from the list. But the list is not a hiding ground for a variety of chemicals of unknowns or uncertain toxicity. It includes nutrients, such as ascorbic acid.

"What is needed right now is for the producers and the users of these substances to take a careful look at the evidence of safety on which they market or use the ingredients. Just as the evidence to support drug promotional claims is thin in many instances, the evidence to support GRAS status of several substances is likely to be equally thin at least in some instances. Industry ought to take the initiative here. But will it? Or will it wait to react to the processes of public examination of its practices?"

William W. Goodrich, Assistant General Counsel, Food, Drug, and Environmental Health Division, DHEW, at the 93rd Annual Meeting of the American Bar Association, St. Louis, Missouri, August 12, 1970.

Elliot L. Richardson
Secretary, U.S. Department of Health, Education, and Welfare

Roger O. Egeberg, M.D.
Asst. Secretary for Health and Scientific Affairs

Charles C. Edwards, M.D.
Commissioner of Food and Drugs

Howard H. Davis
Asst. Commissioner for Education and Information

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PHOTOGRAPHY: Black Star, bottom left 5, 6, 7, 14-18, 26, 27; NAPCA, top 6; Stuart Finley Films, bottom 6, top 11; Pennsylvania Department of Health, 10; Fremont Davis Science Service, center 11; FDA.

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Section 705 [375] of the Food, Drug, and Cosmetic Act.

(a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of the charge and the disposition thereof.

(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

Industrial Chemicals and FDA

by Henry Fischbach, Ph.D

Those responsible for the public health have good reason for their increasing concern about chemical substances that may pollute the environment and, among other things, ultimately find their way into man's food. The recent discovery of toxic amounts of mercury in fresh water fish as a result of contamination of bodies of fresh water is a case in point. Recently there also has been steadily growing concern about the release of polychlorinated biphenyls (or PCB's) in the environment and speculation about why and how these chemical substances enter the environment and eventually man's system through the food chain or through other means.

To assure the safety, purity, and wholesomeness of our food supply, FDA has directed its regulatory and scientific activities to those areas where the possibilities of contamination are most apparent. As new formulations and uses of pesticides and other economic poisons were introduced for agricultural and health purposes, the Agency has concentrated on detecting and identifying these substances in or on foods.

Under its food additive regulations, FDA has sought to assure that substances used in formulating, processing, and packaging foods do not contaminate the food with toxic amounts. Through its responsibility for foods in interstate commerce and imported foods, FDA has inaugurated regulatory, educational, and scientific safeguards to assure that food products in storage or transit are not contaminated by toxic chemicals.

The development of highly sensitive instrumentation and ingenious physico-chemical techniques has enabled man to detect, identify, and measure minute residues of chemicals, both in his own body tissues and elsewhere in the environment and of particular interest in FDA's case, in foods. That these residues exist is a reflection of man's genius for synthesizing new chemical substances to advance his many technologies. Until recent years little consideration has been given to the potential impact of these chemicals on our total environmental cycle. But as these substances become ever more sophisticated and continue to proliferate, it has become essential that man, in his decisionmaking, take into consideration a factor that becomes more and more obvious: these chemicals, many of them in highly stable forms and many others in forms that may combine with other chemical substances to produce toxic materials, cannot be dispersed from our planet and thus must become a part of the environment. Earth and its atmospheric envelope is a closed system!

In this country our control over industrial chemicals is largely in the field of pesticides and food additives simply because of the statutory powers conferred on the U.S. Department of Agriculture and the Food and Drug Administration in these areas. Because of these obligations, the FDA in particular has developed highly sensitive and characterizing methods and equipment with which to monitor pesticides in foods.

It is thus mainly in the food area that we have some data on the extent of pesticide residues in our environment as well as some rather incomplete data about residues in the tissue of man. Little is known about the many residues that result from processing the industrial chemicals used in modern industry, simply because man has not looked for such residues; nor has he developed the appropriate, sensitive methodology by which they can be detected and identified.

Much of the publicly voiced concern over the past years has been aimed at reducing the "known" toxic residues in the environment. This concern is certainly appropriate and efforts are being made to minimize these potential hazards (see article, February 1970 issue, FDA PAPERS, about the report by the Secretary's Commission on Pesticides and Their Relationship to Environmental Health). It is an essential activity, but at least of equal concern should be the planning and deliberation needed to minimize future contamination of the environment.

Chemical substances that are neither pesticides nor food additives are present in our environment and may cause hazardous residues in food and feed. Since some of these industrial chemicals are closely related in chemical structure to stable pesticides and may interfere with our measurement of pesticide residues, the FDA must maintain an awareness of this potential interference and continue evaluating the validity of its methodology for detecting, identifying, and measuring pesticide residues in food. We must recognize that any stable industrial chemical related in structure to the stable pesticides and used in significant tonnage in industrial processes will become a part of the environment and is likely to find its way into food. Aside from man, I consider fish and the sedentary shellfish to be the greatest bio concentrators of certain chemicals. We must determine the nature and extent of this potential hazard and, if necessary, act to minimize it.

A pertinent example of such industrial chemicals in the environment is the PCB's, manufactured by the Monsanto Chemical Company under the trade name,

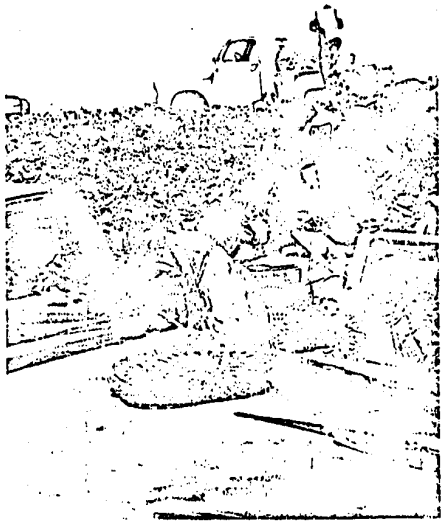
"Aroclors." Several other companies in Europe manufacture similar products under other trade names. These industrial chemicals have certain valuable attributes that are attractive to the many technologies developed by modern man: low vapor pressure, high dielectric constant, beneficial flow property, fire retardance, high stability, etc.

Thus these chemicals have many nonagricultural uses: in paints, transformer fluids, plastics, adhesives, asphalt, tile, etc. With such wide usage it should be expected that traces of these chemicals will enter our watersheds and become concentrated in fish as do such other related chemical structures as DDT. The widespread presence of PCB's in our environment has been established. They were first reported in fish-eating birds and now have been found in fish in the Great Lakes and, in a few instances, in milk and dairy products and even in human fatty tissues.

PCB's are only one of the many industrial organic chemicals undoubtedly present in our environment in such quantity or under such conditions as to cause residues in food and in man himself. We should consider ways to collect sound scientific information on these materials so that decisions can be made based on the net "benefit" to man versus the "deficit."

Among the industrial organic chemicals requiring scrutiny, perhaps the halogenated compounds, such as those containing chlorine, should be studied first. For example, the chlorinated naphthalenes and chlorinated paraffins are widely used in much the same way as PCB's. An FDA food additive regulation (121.2572) permits the use of chlorinated paraffins as cross-linking agents in resins used in coating packaging materials for dry foods. Many other chlorinated industrial chemicals are widely used. Chlorothiophenes, chlorinated pyridines, and chlorinated phthalate and phosphate esters are only a few. The *Federal Register* of April 15, 1970, carried an FDA notice that a food additive petition (FAPOH2519) has been filed by Dow Chemical Company for 2,3,5,6-tetrachloro4-(methylsulfonyl) pyridine as a preservative for food-packaging adhesives. There is an existing food additive regulation (121.2520) permitting use of tri-8-chloroethyl phosphate in adhesives used in food packaging. Hexachlorocyclopentadiene is a building block for chemical compounds that impart fire-retardant features. Chlorendic anhydride in resin-based laminates suppresses combustion and imparts self-extinguishing properties to nonflaming, film-forming resins. Such compounds reduce the hazard to man from fires resulting from an electrical short circuit that starts a blaze in a printed circuit board. On the other hand, these compounds are related to such pesticides as dieldrin and endrin and should be evaluated from the standpoint of a future hazard in the environment, namely, their net benefit or deficit to man.

A host of chemicals are used as plasticizers, a use which seems a very likely source for residues eventually becoming part of the food supply. The leaching of plasticizers from plastic objects in trash disposal

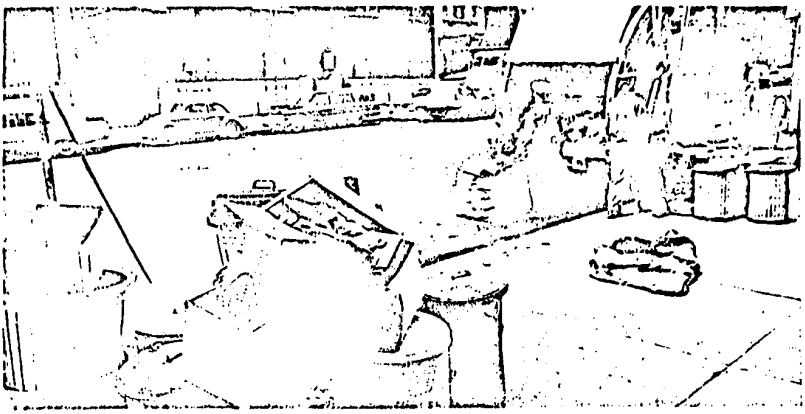


sites and volatilization when plastics are incinerated may result in contamination of streams through scrubbing of the atmosphere by rains, and residues may thus enter the food chain. Many plasticizers are rather stable derivatives of phthalic acid. Almost 784 million pounds of phthalic anhydride esters were produced for plasticizer use in the United States in 1967, according to the U.S. Tariff Commission report, "Synthetic Organic Chemicals," for 1967. A variety of phosphates and other chemicals are also used.

Another likely source of environmental contamination and subsequent residues in the food supply is chemicals used in rubber processing. Aside from waste from processing plants, rubber worn from tires on the highways and subsequent washing of the additive chemicals into storm sewers and streams may result in eventual residues in our food chain. Production of rubber processing chemicals in the United States in 1967 amounted to 264 million pounds, according to the Tariff Commission report. Examples: Total production of thiazole derivatives for this use was over 56 million pounds. Total thiuram derivatives (related to pesticides) was over 14 million pounds.

Only a few examples of widely used industrial organic chemicals have been cited. In 1967, U.S. production of all synthetic organic chemicals totaled almost 105 billion pounds. Of this total, pesticides and related products constituted less than 1 percent, or about one billion pounds. This leaves a huge quantity of synthetic organic chemicals with a wide variety of industrial uses.

Except for PCB's, about which only limited information is available, essentially nothing is known about possible residues of these many nonpesticidal industrial chemicals in man's food supply and in man himself. Furthermore, there is a dearth of information on the toxicology of these chemicals. In most cases, little is known about the toxic effects of low levels ingested over long periods. The only other group for which adequate pharmacology is available is the synthetic



Henry Fischbach, Ph.D., director since February 1970 of the Office of Pesticides and Product Safety, Bureau of Foods and Pesticides, joined FDA in the New Orleans District in 1939.

medicinal chemicals, but the total 1967 production of these chemicals (active ingredients) was only 180 million pounds, less than 0.2 percent of total U.S. organic chemical production.

The evolving PCB's situation is an example of the potential environmental problems associated with man's rapid strides in various technologies. In evaluating the full extent of such ecological complexities, I feel that all available information should be assembled on the volume of use, chemical stability, and toxicity of industrial chemicals related to pesticides. The initial efforts might be directed at the halogenated cyclic chemicals since we have methodology based on years of work detecting pesticide residues containing such compounds. From this information a knowledgeable selection might be made of the chemicals most likely to cause hazardous residues in food, feed, or in man himself. At this point the chemical and physical properties of these chemicals should be evaluated, methods should be developed for measuring the residues in biologic material, and surveys should be made to determine the extent of their presence in the environment. If one of these industrial chemicals is found in food or feed, pharmacological studies at low levels would be essential to determine the potential hazard.

The industrial and scientific community should consider the development and adoption of a mechanism for pretesting new industrial chemicals prior to their introduction into the environment. Stable chemicals that may be used in significant tonnage should be scrutinized by an appropriate panel for their net "benefit" to society when the proposed new chemical is presented to the U.S. Patent Office. Such an evaluation at this point in time should fit into the framework of our economic system with a minimum of disruption.