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Added Chemicals in Foods with Special Reference to the Oil and Fat Industry

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THE Federal Food, Drug, and Cosmetic Act, in effect, bans the addition of any poisonous or deleterious substance to food unless the food cannot be produced without the addition of such a substance. The prohibition is not confined to chemicals. It was the clear intent of Congress to protect food against invasion by undesirable aliens of any character, chemical or otherwise. But most of such invaders are chemicals to the man in the street, and the prevailing practice of using this convenient term has been followed to include them all.

Now the Food and Drug Administration is not opposed to the addition of chemicals per se. Identity standards are replete with examples of their authorization, within prescribed limitations, on an adequate showing of their harmlessness, provided of course their use does not transgress other provisions of the Act which relate to deception rather than to health. But proposals for their indiscriminate use where the above evidence is lacking or inadequate have always been viewed with a fishy eye. In recent years such proposals have been snowballing at a rate that has caused concern in many quarters. Administration concern has been expressed publicly and privately on numerous occasions. A paper (1) was presented before the Association of Food and Drug Officials of the United States in 1946. Later, at the request of Charles Wesley Dunn, general counsel for the Grocery manufacturers of America inc., a somewhat similar paper (2), including more recent developments, was prepared and published. In the former paper a long list of "proposed" antioxidants was presented; doubtless a few more recent ones could be added to the list. There was also a long list of "Quaternaries," which also must have grown considerably by now. In both papers examples were cited where chemicals had been introduced into foods and drugs "with no more sense of responsibility than a skyrocket," and with tragic results. In one case diethylene glycol was used as a "convenient" solvent for sulfanilimide, and the elixir killed over 100 unfortunate sufferers from disease. As if this were not enough, this glycol was also used as a convenient and cheap substitute for alcohol and glycerine for household extracts and flavors. The reasoning perhaps was: "just a little bit of poison won't hurt anybody." More than 100 shipments each of the glycol and of the extracts were hunted down. Later the Division of Pharmacology was able to show that, after two full years of feeding minute doses of either diethylene or ethylene glycol, rats developed kidney and bladder stones, bladder tumors, and other characteristic lesions. Now a rat is very old at two years, but it is doubtful if any persons would care to risk such an outcome by taking a little bit of poison for most of their natural lives. The elixir of sulfanilamide tragedy, more than any one factor, brought about the passage of the "new drug section" of the present Act. Under it a proposed new drug must be shown to be safe for use under the conditions prescribed, recommended, or suggested for it before it may be sold in interstate commerce.

Another tragic episode mentioned in these two papers involved the addition of ortho-cresyl phosphate to so-called Jamaica ginger from an even less worthy motive. Apparently the idea was to make the "extract" behave like the real thing under a routine chemical analysis. This "ginger Jake" was popular in certain arid regions during the prohibition era: that is, it was popular until several hundred victims suffered permanent leg paralysis from this toxic chemical. Other examples are also cited where serious injury from the irresponsible use of chemicals may have been narrowly averted: sometimes by the vigilance of regulatory officials and sometimes, it seems, by sheer luck.

The present Act places squarely upon the manufacturer the obligation of conducting adequate toxicity studies on the chemical he proposes for food use before he sells it to food manufacturers. The Division of Pharmacology has outlined the proper procedure in two papers (3, 4). The earlier paper was abstracted in both the papers on chemicals in foods already mentioned. The great majority of manufacturers have elected to travel the long and difficult road there charted. As might be expected, a few have not.

Concern has been expressed about the ever increasing flood of chemicals proposed for use in food for reasons of convenience, rather than of dire necessity. There are hundreds of them, and on a great many the sum total of knowledge of their harmlessness is precisely nil. It has been estimated that it would probably take the life-time of all the pharmacologists in the country to make adequate toxicity tests on them. From the standpoint of chemical classification these chemicals may perhaps be divided into a relatively small number of groups, but reasoning by analogy between closely similar organic compounds is highly unsafe. Every little substitution has a meaning all its own to the experimental animal, and it may take him two years or so to give us the answer. The answer has to be found. If the manufac-

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turer refuses to accept his responsibility, government must do the job. Of course all of them cannot be tested at once; the ones which seem most likely to be bad actors can be selected with the hope that the guess is right and that the answer will be found before anyone gets hurt, even a little bit.

The present situation calls for genuine anxiety about the future, but not necessarily alarm about the present. There seems to be no immediate threat of acute poisoning or serious impairment of health from added chemicals. But government cannot look everywhere at once, and there may be such a threat that is simply not known. The Administration has not said that there were hundreds of *poisonous* chemicals in actual use, but rather that hundreds of chemicals have been *proposed* for use, on many of which evidence of harmlessness was either inadequate or totally lacking.

The same concern about the present chaotic situation has been expressed, publicly and privately, in many other responsible quarters. The American Medical Association has spoken in no uncertain terms (5). Early in 1948 Mr. Dunn raised the question (6) of amending the Food, Drug and Cosmetic Act along the lines of the new drug section already mentioned. He was thinking mainly of insecticides and their allies, and the toxic nature and the necessity in food production of these chemicals are generally conceded. Also the Act already provides for the setting of safe tolerances in such cases; and a tolerance hearing has been announced for January 17, 1950, broad enough in scope to include all of these pesticides and all fruits and vegetables. This hearing should provide valuable data on the need for different insecticides to the limitations that should be placed on their use in the interest of public safety. But there can be no doubt that serious consideration will be given the possible need of a "new chemical amendment" to hold back the use of chemicals which do not have to be eaten until their toxicity can be assessed. Consumers simply must not be used as experimental animals in the interest of convenience rather than necessity.

The demand for such an amendment has been growing rapidly of late. Another outbreak from an unsuspected source, like those mentioned, would give tremendous impetus to legislative action. The pretesting of a proposed chemical for toxicity is a grave responsibility indeed to place upon a government agency. The Administration has not taken the initiative in proposing such legislation but will support it if it is introduced. The "new drug" provisions of the Act have been most beneficent, and the violations have been few and rather technical. If a "new chemical" provision is added to the Act, there is every reason to expect that it will be equally beneficial and effective.

Perhaps the handwriting is already on the wall, in the form of two substantially identical resolutions that have recently been introduced, one by Congressman Keefe of Wisconsin (H.R. 207), and one by Congressman Sabath of Illinois (H.R. 323). Both call for the appointment of a committee to investigate and study:

> 1. the nature, extent, and effect of the use of chemicals, compounds, and synthetics in the production, processing, preparation, and packaging of food products to determine the effect of the use of such chemicals, compounds, and synthetics a) upon the health and welfare of the nation, and b) upon the stability and well-being of our agricultural economy;
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> 2. the nature, extent, and effect of the use of pesticides and insecticides with respect to food and food products, particularly the effect of such use of pesticides and insecticides upon the health and welfare of the consumer by reason of toxic residues remaining on such food products as a result of such use; * * *
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> The committee shall report to the House * * * the results of its investigation and study, together with such recommendations for legislation as it may deem advisable.

To the oil and fat industry perhaps the chemicals of principal interest are the antioxidants. At any rate government has not heard of any contamination of food oils from oil-soluble organic insecticides used on the parent crops. It is of course possible that lard might be thus contaminated from DDT ingested with the feed or even sprayed on the hogs. Beef fat and cows' milk may be contaminated from such sources. However our surveys, and those of other agencies, indicate that the contamination of supplies of milk and beef is slight indeed. For example, the most that has been found in milk could be characterized as a trace. DDT is no longer recommended for forage crops and dairy cattle or barn sprays. The abandonment of such use should assure its absence from the milk supply. If anyone should wish to make some spot checks of DDT in food oils or fats, government can furnish you with a satisfactory and sensitive method.

Passing mention might be made of the controversy that has raged around chemical bread softeners in the hearing on bread standards—the "bread marathon" someone has called it. In the absence of a "new chemicals law" such a hearing at least provides a forum that is not available for the multitude of foods which are not yet standardized and cannot be for some time to come. There has been considerable testimony, pro and con, on the toxicity of these softeners, which is of course the most important factor of all. There has also been testimony on their effect on bread flavor, their capacity of replacing shortening or milk solids, and on other matters that might have a bearing on whether the authorization of softeners would "promote fair dealing in the interests of consumers," as the standards-making provisions of the Act require. The voluminous 18,000-page Record of this hearing must be studied in detail before conclusions can be drawn.

But to return to the antioxidants. There can be no question of the desirability of these chemicals in lard or in any other fatty food which has a tendency to become rancid or otherwise deteriorate with the lapse of time. But necessity in production is one thing, and preserving of food "against that natural corruption which is its birthright" is something else again. Thus there can be no tolerances for toxic preservatives; all preservatives must be harmless. The Bureau of Animal Industry, with which the Division of Food enjoys close cooperative relations, authorizes the addition of certain chemical preservatives to rendered animal fat or mixtures of animal and vegetable fat. In June 1948 that Bureau authorized the addition of hydroquinone since this chemical had the desirable quality of carrying over its antioxidant properties into baked goods and other foods containing shortening. But the Division of Pharmacology had some misgivings about the adequacy of previous studies upon the toxicity of hydroquinone. Accordingly they proceeded to make some studies on their own account before this chemical found its way into

a host of other foods. Their findings were presented at the April 1949 meeting of the Federation of American Societies for Experimental Biology. An abstract of the paper appeared in "Federation Proceedings" of that organization (Volume 8, No. 1, Part 1, Page 348). The following oral doses in terms of milligrams per kilo of body weight were found to kill half of the group of experimental animals (such a dose is known to the elect as the LD_{50}). As in the bleached flour episode, they used several species of experimental animals. The LD_{50}'s were as follows: rats, 320; mice, 400; guinea pigs, 550; pigeons, 300; cats, 70; dogs, 200. The oxidation products, quinhydrone and qinone, were even more toxic to rats, the LD_{50} for quinone being 130. You will note the wide differences between species. In their second paper on the general subject of toxicity studies, already referred to, the Division of Pharmacology laid down this rule: "Where adequate knowledge of similarity between man and the test animal is not available, it is safest to assume that man is at least as sensitive as the most sensitive species of animals tested."

With the above knowledge available the Bureau of Animal Industry in December of 1948 cancelled the authorization of hydroquinone as a preservative in animal fats and shortening containing animal fats, effective July 1, 1949. At present the Meat Inspection Division of that Bureau authorizes the use of the following chemicals, with a limiting concentration for each:

Resin guaiac
Nordihydroguaiaretic acid (alone or in combination with citric or phosphoric acid)
Tocopherols
Lecithin
Citric acid
Propyl gallate (alone or in combination with citric acid)
Butylated hydroxyanisole (alone or in combination with nordihydroguaiaretic acid or propyl gallate, with or without citric acid or phosphoric acid)

In the light of the present information there is no reason to believe that any of these are to be regarded as poisonous or deleterious substances.

However the evaluation of the toxicity of a chemical to human beings is a difficult business at best. The LD_{50} for babies cannot be determined and they cannot be cut open to see what is happening to their organs and tissues. The animal experiments must be translated into human terms, using great caution and a very large factor of safety. Even when several species are studied, one for its entire life-span, using every tool in the pharmacological kit, the final judgment of harmlessness must still be a cautious one. This is no matter for guesswork, wishful thinking, or imperfect analogies, and there has been far too much of this sort of thinking in the past. Fortunately Pollyanna optimism is not nearly as prevalent today: there have been too many wrong guesses, many of which are matters of general knowledge.

At best one can never be dead sure that a chemical is harmless even if it has enjoyed long use. Take the nitrogen trichloride process for bleaching and maturing flour for example. This had been in use here and abroad for some 30 years with no evidence of toxicity. Then, late in 1946, came a bombshell in the form of a paper by Sir Edward Mellanby, an English scientist of international reputation. He reported that dogs fed on flour so treated developed what is commonly called running fits. His findings were soon confirmed in America, by this Administration and by the owners of the process. Cats, rabbits, and ferrets were found to be similarly affected, but other experimental animals were not. While no evidence that humans are affected was obtained, then or later, nobody wanted to wait another 30 years to find out. The use of nitrogen trichloride was promptly abandoned. Can anyone wonder that pharmacologists are inclined to be profoundly pessimistic? Rather than being dogmatic about the harmlessness of a chemical, they agree with the cautious Vermonter who looked at a cow on a mountain side and said: "Well, she's white on this side."

And now a word, in closing, about the views of the courts on the meaning of "poisonous or deleterious" as used in the Act. Late in 1945 an injunction was granted against the interstate shipment of popcorn (of all things) lubricated with mineral oil, on a showing that mineral oil robbed the system of fat soluble vitamins and produced other undesirable effects. The last of the findings of the court is quoted:

> That the popped popcorn which is the product of the defendant contains mineral oil in sufficient quantities to be harmful; that such mineral oil is a deleterious substance which renders the popcorn injurious to health; that the popcorn is therefore adulterated within the meaning of the Food, Drug and Cosmetic Act.

Shortly afterward the trade was placed on notice, with a warning to salad dressing manufacturers that they could no longer put out "non-fattening" dressings under the sheep's clothing of special dietary foods. Most of them listened, but a few rugged individualists did not. A number of shipments were seized without contest, but recently one manufacturer elected to fight. On evidence similar to that introduced in the popcorn case it took the jury (and a New England jury at that) less than half an hour to decide that the salad dressing was deleterious within the meaning of the Act. It seems quite unlikely that the courts are going to consider "just a little" injury to the consumer as one of the trifles that, according to the Latin proverb, the law does not concern itself with.

REFERENCES

1. Quarterly Bulletin, Association of Food and Drug Officials of U. S., October 1946.
2. Food, Drug, and Cosmetic Law Quarterly, December 1947.
3. Woodard and Calvery, "Industrial Medicine," January 1943.
4. Food, Drug, and Cosmetic Law Quarterly, September 1949.
5. Journal American Medical Association, August 28, 1948. Food, Drug, and Cosmetic Law Quarterly, December 1948, March 1949.
6. Food, Drug, and Cosmetic Law Quarterly, June 1948.

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