

UNIVERSITY of ILLINOIS
COLLEGE of AGRICULTURE
AGRICULTURAL EXPERIMENT STATION
URBANA, ILLINOIS

DEPARTMENT
of HORTICULTURE

January 24, 1936

Dr. Robert A. Kehoe, Director
Kettering Laboratory
University of Cincinnati
Cincinnati, Ohio

Dear Dr. Kehoe:

Attached is a copy of my letter to Mr. L. S. Hitchner, President, Agricultural Insecticide and Fungicide Association, in response to his request for information concerning developments since Professor Pickett and I saw him in December.

I shall appreciate it if you will read my reply, in spite of its length. I have put a lot of thought (that is, from my standpoint) on this letter.

If anything that I have said needs clarification or emphasis, please write to Mr. Hitchner directly. I do not know just when he intends to present the matter to his organization; however, it will be within a few days.

Yours very truly,



WAR:MH
Enc.

Chief in Pomological Physiology

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January 24, 1936

Mr. L. S. Hitchner, President
Agricultural Insecticide & Fungicide Association
285 Madison Avenue
New York City

Dear Mr. Hitchner:

After seeing you in New York, Professor Pickett and I called upon Mr. F. E. Wormser, Secretary and Treasurer, Lead Industries Association, 420 Lexington Avenue, New York. We also talked with Mr. Robert F. Wilson, in the office of the Associated Grocery Manufacturers of America, 205 East 42nd Street, New York. The Lead Industries Association is financing a \$10,000 fellowship at Harvard. Mr. Wormser invited us to make a trip to Harvard with him. We made the trip, and discovered some interesting facts which confirmed us in our belief that experimentation of the type that we had outlined would be desirable. Equally encouraging was the fact that the men who were doing the work at Harvard (Drs. Aub, Fairhall and Calhoun) agreed entirely with our general conception of the situation as a whole. You probably know that Aub and Fairhall have been working on the biochemistry of lead for ten or twelve years. What they say at Harvard carries a great deal of weight.

Mr. Wormser said that their budget for the year was already made up, that lead arsenate was not a major product of theirs, and indicated that in all probability they would not contribute. However, it is my opinion that a contribution from them in the future would not be an impossibility.

After my return to Urbana I wrote to Mr. Wormser, telling him what we were doing and hoped to do. I am quoting a paragraph from his reply:

"I am particularly pleased that you are getting in touch with the apple growers, as I firmly feel that their position, so far as the spray residue is concerned, will not be improved until they have marshaled sufficient scientific evidence to answer the allegations of the various State and Government Departments about the toxicity of lead arsenate. Needless to say, we shall be glad to help you all we can and I hope you will keep us posted with whatever program is finally adopted, for we should indeed like to know what progress you make with your investigation. At the same time, if anything should occur at this end which I think will be of interest to you, I shall pass it on promptly."

Mr. Wilson, of the Associated Grocery Manufacturers, told us that many of their constituent organizations were interested in lead toxicity. They have a fellowship at Yale,

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with Dr. George R. Cowgill, Associate Professor of Physiological Chemistry. Mr. Wilson asked me to write to him when I returned. He said that he would then take the matter up with Mr. Willis, President of their organization. I wrote Mr. Willis, but have not yet received a reply. I know that they are greatly interested in all phases of the lead problem, but I do not know, of course, how much they would be interested in lead arsenate experimentation. Presumably they will be decidedly interested, although they may think that the lead work at Yale is enough. (This may be a good place to say again that the only way to settle the lead tolerance problem is direct work, with humans.)

Professor Pickett and I had a very interesting and instructive visit with Aub, Fairhall and Calhoun at the Huntington Memorial Hospital in Boston (Harvard). Their work and the work at the Kettering Laboratory has had a great deal to do with modern conceptions of the behavior of lead in the body. It should be said, also, that a great deal of this work has been done since 1926, when the limit of .014 grains of lead per pound of apples was set by the physiologists advising the Food and Drug Administration. Of 38 articles referred to in a recent paper by Aub on the biochemical behavior of lead in the body (Journal of the American Medical Association, January 12, 1935) 9 had been published in 1931, 6 in 1932, and 8 in 1933. The subject is therefore a very live one.

You might have occasion to use a very brief general summary of the most important facts in lead biochemistry. My attempt in that direction follows:

Lead is ingested in minute amounts in the normal diet and excreted in quantities which are, in the long run, equivalent. Under normal circumstances, lead is not cumulative except that very small amounts are normally stored in the bones with increasing age. A large part of the lead in the diet probably passes through the body unabsorbed; inhaled lead is much more dangerous. When comparatively large amounts of lead are ingested or inhaled, which is likely to happen in certain industries, accumulation takes place. Storage is in the bones, along with calcium. After removal from exposure, (for example, when a factory worker exposed to white lead dust leaves the factory) stored lead is normally slowly excreted, also along with calcium. If a metabolic upset results in the rapid liberation of large amounts of stored lead, very deleterious effects may result. The rate of liberation of lead from the bones can be regulated, however, by regulating the supply of calcium in the diet or blood, which is the basis of medical treatment. The amount of lead arsenate or, as a matter of fact, of any other form of lead, that can be ingested before storage takes place is unknown. Several factors probably enter, one of which is the chemical and physical nature of the lead compound itself.

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In this connection, also, I am sending you two reprints from the Kettering Laboratory and am writing to Dr. Aub, asking him to send you a reprint of the article to which I have just referred. The supply of the larger reprint from the Kettering Laboratory is exhausted; otherwise, I would send you several copies.

Since we talked to you, it has become more and more apparent to me that the effect upon ordinary apple consumers of the normal consumption of apples, bearing the amount of lead at present permitted, should be investigated. The most logical way to find out whether danger exists is to look for instances of injury. This procedure was used when the United States Public Health Service investigated the tetra-ethyl lead gasoline problem. A failure to find actual instances of lead poisoning among consumers of ethyl gasoline was considered a good reason for permitting its use. To quote from the report of the study, published in Public Health Bulletin 163, Treasury Department, United States Public Health Service, no. 109, 110, 1926, "In the regions in which ethyl gasoline has been used to the greatest extent for a period of between two and three years no definite cases have been discovered of recognizable lead poisoning or other diseases resulting from the use of ethyl gasoline. In view of these conclusions (which include the result of a study of automobile users and garage employees) your committee begs to report that in their opinion there are at present no good grounds for prohibiting the use of ethyl gasoline of the composition specified as motor fuel, provided that its distribution and use is controlled by proper regulations." (The regulations apply to plants which manufacture tetra-ethyl lead and blend it with gasoline.)

In this connection, two very important facts are fundamental. The first is that lead, in amounts below a certain minimum, is not a cumulative poison; the second is that lead normally disappears from the body. If these general facts had not already been established, we might assume that the investigation would be certain to reveal almost universal lead poisoning. Since they exist, we may perhaps assume that lead poisoning is correspondingly rare.

Dr. Kehoe, Director of the Kettering Laboratory, has already included a "field investigation" in his plan, which he drew up in September, 1935, but I did not realize its comparative importance until recently.

You are, of course, familiar with the objects of the laboratory investigation. This part of the investigation also has assumed more importance as I've thought it over. In the third paragraph on Page 2 of the mimeographed copy of the paper that I gave at Hartford I quote Dr. White's reference to the toxicity of lead in drinking water. The 0.1 milligram of lead which, ingested daily, is supposedly capable of causing chronic poisoning is very much below the average daily ingestion of lead in the food, which, as shown by work at the Kettering Laboratory, amounts to approximately 0.25 mg. (approximately .004 grains).

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The toxicity of lead in drinking water, therefore, seems to be abnormally high. It is another demonstration of the fact that the toxicity of each individual lead compound should be determined individually and that it should be ingested with the food with which the compound naturally is taken into the body. There must be a reason for the extreme toxicity of lead in drinking water, because a greater amount of lead in food is not toxic. Also, the fact that a greater amount of lead in food is not toxic is a good reason for not basing the tolerance for lead on apples and other food on the toxicity of lead in drinking water. However, this seems to be a possibility, judging by the references by an official of the Food and Drug Administration (Mr. White) to its possible importance. If that were done, the reduction in the lead tolerance would be very drastic. I should also say that the work already done at the Kettering Laboratory, which ought to prevent such a reduction, has been done without expense to the interests most directly concerned; furthermore, without active effort on the part of scientifically qualified, alert and informed individuals a defense on scientific grounds would go by the board--it would never be formulated.

After seeing you, Professor Pickett and I visited entomologists and chemists in Washington, to be reasonably certain that no substitute for lead arsenate was just over the horizon. There has been a great deal of activity by entomologists and manufacturers, as you, of course, know, to find a substitute. Overlay and others in Washington State have hopes of calcium arsenate with zinc sulfate and lime as a safener. We know, however, from experiments here at Illinois that zinc sulfate and lime cannot be used in this climate as a safener on apples, because the zinc russets the apples, and we know that calcium arsenate is variable in its properties and has other disadvantages. It is to be hoped that a substitute will be found, because such a discovery would settle the whole thing at once, but, to put it very conservatively, there is nothing in immediate prospect for general use.

Mr. R. G. Phillips, Secretary of the International Apple Association (whose address is 1108 Mercantile Building, Rochester, New York) and I also called upon Dr. Campbell, Head of the Food and Drug Administration. I asked him if he would accept the results of the experiment that we proposed. He said that he was anxious to secure any scientifically acceptable information that would help to settle the problem. I asked him if he would take a part in the organization and conduct of the experiment. He said that he would not, that his division would conduct an investigation of its own, and that two entirely separate investigations would be more desirable than the one investigation that would result if there were close cooperation. In their investigation commercial interests of any sort are not to be represented, so that the result will be entirely free from bias; that is, it will be based purely and simply upon biological and chemical facts.

I have had quite a little correspondence with Dr. E. E. Ware, of the Sherwin Williams Company, about the

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proposed Kettering Laboratory experiment. Dr. Ware's last letter expresses his hope that the attitude of the Food and Drug Administration toward cooperation can be changed. Without Dr. Ware's permission and with ~~diff~~^{my} apologies to Dr. Ware on that account, I am quoting his letter and my reply.

"Dr. W. A. Ruth,
University of Illinois,
College of Agriculture,
Urbana, Illinois.

Dear Dr. Ruth:

I thank you for your letter of the 26th enclosing copies of your paper, "The Spray Residue Situation".

Mr. Gunderson and I have discussed the whole situation several times and both of us feel that a conference with you might result in a different understanding on our part.

I sincerely wish there could be some neutral ground on which producers, consumers, and federal agencies could get together. We could all agree to check our personal prejudices at the door along with our hats and discuss matters of mutual interest from the standpoint of public welfare. Why should it be necessary for Dr. Campbell to conduct semi-secret investigations, apparently to get ammunition with which to combat industry if it should attempt to promote sale of a product that in his opinion is inimical to the public interest? Why couldn't such governmental investigations be conducted under the guidance of a committee, membership to be chosen from the U.S. Department of Agriculture and Experiment Station staffs; Growers' Association membership, and manufacturing industry. One might even consider the advisability of asking the Farm Chemurgic Council to cooperate.

It seems to me that we must concentrate on the problem of promoting a better understanding and mutual respect between Federal Research and Regulatory Bureaus on the one hand and agricultural and industrial organizations on the other. There must be some Moses who can lead us out of the wilderness of misunderstanding.

Very truly yours,
THE SHERWIN-WILLIAMS COMPANY
E. E. Ware (signed)
E. E. Ware

EEW:w

My reply to Dr. Ware follows:

"Dr. E. E. Ware
The Sherwin-Williams Company
Cleveland, Ohio

January 9, 1936

Dear Dr. Ware:

I greatly appreciate your letter of January 2, and I understand your attitude. I do not know what can be

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"done along the lines that you suggest--i.e., to convince the Food and Drug Administration that they should conduct the investigation of lead toxicity under the guidance of a committee, chosen to represent the experiment stations, federal horticulturists, manufacturers, and fruit growers, as well as the Food and Drug Administration itself. I agree with you that prejudices would be checked at the door. I am certain that the fruit growing industry would have that attitude if it were allowed representation.

My interview with Dr. Campbell and Mr. Phillip's opinion of him have made me sure, however, that any investigation that they conduct will have as its sole purpose the ascertainment of facts. On the other hand, I can easily see that, if it is conducted without the representation of interests other than enforcement officials, it will be open to the criticism that you have in mind--that its supposed purpose will be "to get ammunition".

Also, it is certainly true that this investigation can be planned in such a way that it will be fundamentally (scientifically) satisfactory or unsatisfactory to all interests, and that the only way to insure satisfactory planning is to have all interests represented. For example, the lead arsenate on washed apples is probably much less toxic than acid lead arsenate, because of the weathering that has taken place on the fruit, which tends to transform it to basic lead arsenate, and because the washing process probably removes the particles that are most easily dissolved. Therefore, washed apples should be used as one source of lead arsenate. A toxicologist or biochemist not experienced in horticulture would overlook this point. He might even imagine that he would be more scientific if he were to use pure acid lead arsenate because it is undecomposed and uncontaminated. He might think, also, that he could get the purest lead arsenate from a chemical supply house. There are probably a number of important points of that sort. Most important of all, perhaps, is the point that field investigations should constitute an important part of the investigation, by which I mean an examination of consumers for evidences of lead poisoning. I think, as you do, that representatives of the various interests would participate in a perfectly fair way; presumably, also, the best companies, horticulturists, fruit growers, etc., could help the Food and Drug Administration actively after the facts were established.

I have attempted to state the situation as you see it in my own words. As far as I know, my statement is complete, and the argument is absolutely sound.

The arguments for conducting a separate investigation at the Kettering Laboratory can be stated very briefly by saying that it would be exactly that kind of an investigation except for the cooperation of the Food and Drug Administration in planning and conducting the work, that a laboratory is miraculously at hand for doing the work, that most of the expense and effort would therefore be obviated because we would not have to work from the ground up, that the results of the "

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Mr. L. S. Hitchner

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"experiment would be acceptable to the Food and Drug Administration, as well as to other interests, and last, but not least, that we would not have to ask the Food and Drug Administration to adopt a policy with which they are not already in sympathy.

I would be assuming entirely too much if I were to say, as a result of my brief interview with Dr. Campbell, that I have expressed his final attitude. As I told you, I think that he is anxious for all the help that he can get in arriving at the truth.

Yours very truly,

W. A. Ruth

WAR:MH

Chief in Pomological
Physiology

This long letter, I believe, just about exhausts everything that has occurred recently in this connection. I might add, however, that I learned indirectly a day or two ago that the American Can Company is interested in lead in Certo and other foods. I learned this through the representative of a firm which makes apparatus used in lead analysis. Doubtless many organizations are interested more or less directly, whose interest is not known to us at present.

Before I conclude my letter I should add that all of the scientists with whom I have talked about this experiment, both before and after seeing you, agree without qualification in the scientific soundness of the proposal. For example, Dr. Roger Adams, Head of the Chemistry Department here, in a conversation last night spoke very highly of the analytical work at the Kettering Laboratory. It was, incidentally, Dr. Adams who, as President of the American Chemical Society, has a very wide contact with chemical research, who gave our first hint of this opportunity. Horticulturists and fruit growers are strongly in favor of experimental work. (See the attached editorial, "The Residue Problem", from the American Fruit Grower, written by Professor Gourley, Head, Department of Horticulture, Ohio State University and Dr. M. J. Dorsey, Head, Division of Pomology, University of Illinois.)

I thoroughly agree with Dr. Ware in his statement that the United States Department of Agriculture, the state experiment stations, the fruit growers, and the manufacturers should all be represented in the experiment, as my reply to him indicates. It is an interesting fact that the membership of the American Pomological Society is drawn from exactly these sources. It is the society that can most logically be expected to organize the experiment and to keep it going, which is just as important, because its interests are commercial as well as scientific. Furthermore, as any one who attended its December meeting could not fail to realize, it is a very active society.

Yours very truly,

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Chief in Pomological
Physiology

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"no.

Mr. L. S. Hitchner

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P. S. I am going to go through the two reprints that I am sending you, transferring milligrams to grains, to which we are now accustomed in this connection.

W. A. R.

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