

March 29, 1948

Mr. C. n. Van Hartesveldt,
Thompson Vita-Meter Corporation,
23555 Euclid Avenue,
Cleveland 17, Ohio.

Dear Mr. Van Hartesveldt:

Since my telephone conversation with you I have given careful consideration to what I could recommend in the way of experimental work at this time on the problem of your anti-detonant mixture. The problem is just a little complicated by a number of considerations, and it seems wise, therefore, to set down my point of view in writing, so that some of these complications can be eliminated so far as this is possible. I should not want you or your associates to feel that I am being unduly critical, or that I am dodging my own responsibilities in any way. Rather, I speak out of uncertainties with respect to where we are going and how we can expect to get there. It seems highly important to me that there be a well defined step-by-step procedure in future developments, whereby misunderstandings and difficulties can be avoided as far as possible. It is especially important that no one be asked to assume any risks in connection with these developments, without there being adequate means of checking them as they go. This is one of the inevitable problems of a research and development program in which numbers of individuals are involved. I happen to be somewhat in the middle, and therefore if I speak somewhat out of turn, I am sure you will understand that I am merely trying to do my best for everybody.

The hygienic problems associated with this problem may vary considerably with the following factors: -

1. The composition of the solution or mixture to be used;
2. The precise manner in which this is to be handled; and
3. The extent to which such handling presents difficulties which require medical supervision, or regulations which will ensure uniformity of handling.

As I see the picture at the present time we are not certain as to any of the foregoing points. The composition of the mixture may have been decided upon, but it appears that further consideration is being given to this, and that it may be changed. If this is the case, experimental work on our part would be wasteful at this stage, since any change in the composition of the mixture would require us to begin all over again. The principal problem with which we are concerned at this time is that of the possible absorption of tetraethyl lead through the skin as the result of skin contact with the mixture. It will do absolutely no good to investigate anything but the final mixture as it is agreed upon, since any change in the mixture may effect the absorbability of

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tetraethyl lead through the skin.

It is equally true that any change in the mixture may influence very importantly the factor of vaporization of tetraethyl lead from the mixture. This is our second concern from the hygienic viewpoint. This will have to be investigated by physico-chemical methods, rather than by animal experimentation, at this time, since it would require months of difficult and costly experimentation to obtain any answer to this problem by toxicologic methods. The extent of the vaporization of tetraethyl lead will have to be determined by properly designed laboratory experiments, comparable to those carried out by Calingaert on gasoline-lead mixtures. (It is my understanding that Calingaert has in mind the conduct of such experiments, or at least that he is willing to do so, if I recommend it. It is rather important, therefore, that we establish who is to do what and for whom.)

The foregoing parenthesis introduces a problem which bothers me. The personnel of Ethyl Corporation have been asking me various questions about how to proceed, and it is manifest that they have every reason to be greatly interested in this whole matter. The safety division have been called upon to assist in certain ways, in that they have to approve any operations related to making up mixtures for experimental purposes. The laboratory personnel have talked with me from time to time, and they are considering various aspects of this problem. Some of the executive group are disturbed. All of these things may have been worked out by someone, but there does not seem to be a coordinated approach to this problem which would enable us to handle all angles of it properly. Therefore, I cannot but feel that it would be very wise if representatives of the various people concerned were to get together for their mutual information, and perhaps for the development of a coordinated approach to an adequate and properly supervised program of development. I do not look with favor on setting up experiments that involve the exposure of the personnel of petroleum companies or transportation companies, without a degree of supervision that will enable us to know what is taking place. One cannot assume that this is a safe procedure, and therefore even the experimental or developmental program has to be thought through very carefully and supervised carefully. I feel that this is not being done, and that your company and those associated with it are taking undue risks in proceeding with an experimental program involving the use of tetraethyl lead.

Now as to your letter of March 23 and our advice on the matter of our own experimentation. Just as soon as the mixture you are to use has definitely been decided upon, we should undertake some experiments whereby we determine the extent of the absorbability of tetraethyl lead out of this mixture through the skin of animals. This will involve applications made daily over a period of several months upon the skin of animals, after which these animals will have to be killed and each of their tissues analysed minutely for its lead content. This will require something like ten analyses per animal, and it seems likely that 20 or 30 animals may be required in test and control groups in order to give any information comparable to that available

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in the case of gasoline containing tetraethyl lead. Some tentative information could be obtained within a period of three months, but these observations could be carried on for about six months, in all probability. The cost of the work will approximate \$100.00 per animal, certainly not less. This is all of the experimental work that I should anticipate doing at once. Work on the inhalation problem will probably have to be undertaken later.

In the above connection it seems to me quite apparent that this whole problem will have to be discussed at some reasonably early date with representatives of the U. S. Public Health Service. Everything that has to do with the use and distribution of tetraethyl lead on a community basis is a matter of direct concern to them, and the tetraethyl lead industry is pledged to bring to their attention all matters of consequence related to changes in the use of the product. I have had a very close association with the Public Health Service in this and in other matters for many years, and it will be necessary for me to discuss this with them at an appropriate time. So long as this is in the experimental stages, it seems advisable merely to inform them of that fact and to say that experimental information will be brought to their attention. However, if commercial distribution on any other than an experimental basis, were to come about without their knowledge, this could easily be regarded as a breach of good faith. As you can see, there are a number of aspects to this problem which require that developments be made in an orderly fashion on the basis of the best possible information.

My specific recommendations at this time are:

1. That a conference of the interested technical personnel, with ourselves included, be called together at an early date so as to decide upon procedure;
2. That a coordinated program of technical, hygienic and field experimentation be adopted;
3. That since the hygienic experiments indicated above will be prolonged, of necessity, a binding decision should be made at the earliest possible time on the composition of the mixture, so that our program of experimentation can begin. At that time an initial appropriation of about \$5,000.00 should be made available, so that we can proceed without delay in obtaining the primary facts on the possibility of skin absorption.

You may feel that I am taking a somewhat different position than that represented to you and Mr. Gay in our conference of some time ago. I think this is not quite the case, since two new factors have entered into the situation. At that time, I believed that the composition of the mixture had definitely been determined. This seems not to be the case. Moreover, I felt that a considerable period of well controlled experimental developments, without any attempt to go beyond this stage, was to be expected. This also seems not to be the case. This fact gives me some anxiety. Consequently it seems wise to speak my mind as fully and as frankly as possible.

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Cordially yours,

Robert A. Kehoe, M. D.

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P. S. I neglected to say that in my feeling I or one of my associates should visit you in Cleveland soon, so as to find out just how you propose to proceed with the Yellow Cab group, so we can plan to supervise any individuals who may be involved in potential lead exposure. We should see the men before they are exposed and from time to time during their exposure, so as to surround them with proper safeguards and to obtain all pertinent information that can be obtained. I shall be in Boston the balance of this week, but will be available in Cincinnati on Monday, April 5.

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