April 26, 1960

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Dear Red:

Just in case you wish to introduce something on tetramethyl lead into your book, I think I had better give you the whole story. The report from the Haskell Laboratory is just a fragment of it. I have a copy of it incidentally. I believe John Zapp and his group are making some further study of it.

Back in the late thirties, Ethyl Corporation became interested in lead alkyls that would have greater volatility than tetraethyl lead, for technical reasons, among which was a desire for a more even distribution of the lead compound among the cylinders of internal combustion engines. The matter of getting the heavier ends of gasoline, as well as the tetraethyl lead (which boils at about 200°C, and has a low vapor pressure, in the physical sense), evenly distributed has long been a problem. A series of alkyl lead compounds was investigated technically, and we in The Kettering Laboratory examined several of them (work which has not been published, partly because it was incomplete and partly because we were too busy with other things). We, as well as the technical people in Ethyl Corporation, decided that tetramethyl lead was too volatile to use with safety, because it would vaporize from gasoline at too high a rate - 100 times, perhaps, as rapidly as would tetraethyl lead under the same circumstances. This killed the proposed use until recently, when the difficulties encountered by certain automobile engines became more pronounced.

Last year this problem was dumped in our laps again, and of course, now, duPont is interested also. Some of the people in the petroleum industry would not take my word as to the potential risks, and, fortunately, insisted on having better and more practical evidence. I shall not go into the details of this, but I agreed that I could be wrong in the quantitative sense, and proposed a field (use) investigation, which has now been carried out. I was wrong, quantitatively, and I admit it freely, for the difference between tetramethyl lead and tetraethyl lead under the conditions that prevail in the handling of gasoline in the U.S.A., with respect to what gets into the air breathed by the people concerned, appears to be of the order of three to one or less, instead of one hundred to one. I had failed, as we so often do in extrapolating from the physical properties to the practical situation, to take properly into account (1) the length of time within which

the physical factors operate, and (2) the extent and the speed of dilution of escaped vapors with air under ordinary conditions.

It is now apparent that tetramethyl lead can be used, and by the time you receive this letter it use on the West Coast will have been initiated and announced. I have talked with the national, state and local authorities concerned, and there will be, I believe, no objection to this. The initial evidence for its safety is found in a field survey which we carried out. I am sending you a copy of this report in which, deliberately, there is no reference to the site at which the observations were made, (we are setting up a schedule of monitoring observations on the West Coast which will continue through the year, so as to check the preliminary survey.)

I am also sending you a brief resume of the preliminary toxicologic observations which we made years ago on tetramethyl lead, tetraethyl lead, and the mixed alkyls in between them. There is much more information available than is contained in this brief report, but I am not putting it out for the reasor that we are reexamining the toxicological characteristics of both TEL and TML, and I don't want to have to take back anything that we have written into the literature. There are some loose ends here that necessitate this re-examination, but it appears that there is no very great difference between these two compounds, toxicologically.

Now as to the report of which you have spoken. It is highly preliminary, and while I am not suggesting that it is in error as far as it goes, it is not a proper basis for considering the problem of lead intoxication in this relationship, either in industry or in the community generally. Moreover, there is reason to believe that the differences in the behavior of animals, in response to the absorption of these two materials, is a matter largely, if not wholly, of quantity. For example, we have observed that central nervous excitation occurs in response to the inhalation of both of these compounds but at different levels of concentration in the air, whereas, both appear to be capable of inducing depressive effects, but also at different levels of concentration in air. It is well, therefore, to reserve judgment until more information is available. All told, we know little about TML beyond the acute toxic manifestations induced by brief severe exposure. We need much more than this, as no one knows better than yourself. I have my fingers crossed also about the pathology of poisoning by these compounds. Incidentally, the microscopic pathology this report is referring to was observed and interpreted by our friend Schepers. Hold everything! You will remember that I pointed out to you long ago, that there are no residual effects so far as clinical manifestations can reveal them of encephalopathy due to TEL. We must be very careful, therefore, in our interpretation of minute microscopic findings in the central nervous system of animals. People like Schepers, who like to find and publish and make much of changes of this type, must, I fear, be dealt with cautiously. I am afraid John Zapp does not know this, but it is not because I have not warned him.

Incidentally, for your private information, the TML being used on the West Coast is Ethyl's product, for the reason that Ethyl, at this particular time, is the only manufacturer with a satisfactory method of production. This will

not exist long, but TML is Ethyl's baby, of long standing. I can assure you that if you want to make some reference to it in your book, you need have no hesitation in doing so. Just don't stick your neck out too far with respect to precise toxicological information.

One other point, I think I can promise you that within the year, TML will have considerable use in the U.S.A., and its use will have spread to western Europe at least. It is needed in certain parts of Europe more than it is here. The only reason for regarding information about it as confidential, for a time, was that the Company on the West Coast agreed to initiate its use before anyone else, if it could be done without revealing that fact to anyone else in the industry. Don't quote me on this please, for I've been holding the line carefully, and have not told anyone else what I've told you. I can do it now since the information about the commercial use of this product is to be released on April 25th.

Sincerely yours,

Robert A. Kehoe, M. D.

Dictated but not read

RAK:ss

Enclosures