

July 8, 1959

Dr. Philip Boyd
The Associated Ethyl Company Limited
Medical Services
20 Berkeley Square
London, W.1.

Dear Philip:

I hasten to reply at once to your letter of July 3rd concerning the possibility of the use of tetramethyl lead in gasoline in order to improve the distribution of lead throughout the cylinders of the internal combustion engine. I shall merely refer in passing to the other matters in your letters, for I would have to give more thought to them - especially to the problem of policy in connection with a change in the status of your successor - before offering an opinion.

The desirability of the use of a more volatile lead compound in certain types of gasoline has been with us for years. It was considered by Ethyl Corporation years ago (in the middle thirties), and Dr. Machle carried out a series of toxicologic experiments at my instigation, in order to get some idea of the potentialities for harm that might be associated with the relative toxicity of the lead compounds formed by the methyl and ethyl radicles singly and in various combinations. I send you herewith a report recently put together, because of the recurrence of interest in this matter, which summarizes the results of the toxicologic experiments. This work was never prepared for publication, and indeed no full report was prepared. There are more data, especially the results of analyses of the tissues of animals, and there was a fairly extensive series of experiments that are not described in detail, but the essential facts, insofar as they are reasonably definite, are found in the brief summary. I should say, from these experiments, that the differences between the several compounds are of moderate significance, from a toxicologic viewpoint, and that the hazards associated with their use as antiknock materials would be much the same but for the differences in their volatility. This is by no means certain, for there seems to be less danger from the percutaneous absorption of TML, and it also seems that the concentration in air required to kill is appreciably higher. I have some idea as to why these things are - or appear to be - true,

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but from the aspect of prolonged exposure to the lead alkyls, of their distribution and degradation in the body, and of their accumulation in the tissues, my principal concern relates to the concentration in air under the conditions of the daily work. I am very much afraid of TML on this score, since its effective volatility, under ordinary conditions of the handling of gasoline, may be as much as eighty times that of TEL. This has nothing to do with intrinsic toxicity, which I take to be not too different, but with opportunity for exposure, i.e., with practical hazard.

I speak of volatility out of gasoline, rather than in relation to the manufacturing hazard, because I am concerned about the hazard to gasoline handlers. Observations have been made in the Detroit Laboratories as to what this volatility means in practice, at my request. The data show that the vaporization of TML out of gasoline may be as much as eighty times that of TEL under suitable conditions. No one knows just what this would amount to in commercial practice, but in 1937, I discouraged the further consideration of the exploitation of TML and even of a much less volatile mixture of lead alkyls. The technical people in Detroit agreed with me, and we wrapped up the whole project (which had quite some commercial advantages in its favor) in mothballs.

The matter has now been brought to life, through the technical work in a number of oil company research groups that have re-discovered the advantages of the use of a more volatile lead compound, but who do not have the background of the hazard to deter them. Meanwhile the technical problem has developed further and the prospects are such that I now have no doubt that the whole question must be reopened, examined more fully and put to the actual test of use. We shall no longer be able to discourage this development by the rational presentation of the reasons for our belief that it is unduly dangerous. We shall have to prove or disprove the existence of such dangers. Preliminary work is under way in the United States at the present time on this very point. The groups involved are committed to a policy of secrecy at present, so that I am not at liberty to describe the experimental approach. All I can say is that a trial use of TML in gasoline on a very small scale is under way, and this may lead to a more extensive set of observations. I believe the entire matter will be opened up for investigation, and I anticipate that the entire industry eventually will be concerned. Certainly, if it turns out that TML can be used with safety - this is unlikely but not impossible - it will be used extensively.

I am in an awkward spot in this whole matter and I have to exercise the greatest discretion in what I say. What I have said to you is in the realm of the affairs of this Laboratory, and the

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report I send you is that of the Laboratory. The developments within the several units of industry concerned in the U.S.A., as I indicated above, are confidential. The essential problem however, can be discussed, and in due time I shall be able, no doubt, to consider with you such matters as the manufacture, distribution and use of such a product as can safely be used. Meanwhile, although I am not suggesting that this is a confidential letter, I do suggest that anything I have said about the commercial aspects of this matter be treated with discretion insofar as quoting me is concerned.

The matter of your successor is a problem, not so much from the aspect of who it should be, but from that of the manner in which his job is to be done. It is my personal belief that the medical director or chief medical officer must, in his own right, be a physician in practice, or a research worker, if he is to maintain his professional status with productivity and satisfaction. Otherwise, he may have to be in industry only part of the time. An administrative job, in the orthodox sense, may be sufficient for some people, but it would not do for me, I'm sure. Consequently, I have been pleased that Ethyl Corporation has given its enthusiastic approval to the continuation of its Medical Department in this Laboratory, where the Medical Director and his associates can engage in other medical work. The man (or men) who has the responsibility for the people engaged in research development and manufacturing, has no professional problem, but the man who spends his time in conferences, which are a necessary part of his job, and in directing others, which must be done, is too likely to lose most of the professional skills that are precious to him. There should be some manner by which this problem can be met and solved. Without being entirely sure of my ground I would suspect that the chief medical man of Associated Ethyl should be located at the principal manufacturing plant, with enough competent help to enable him to go to London as frequently as might be necessary, or to go elsewhere, as required, to look into or to direct other medical affairs of the Company. His schedule could then include his share of the clinical work, and the supervision of clinical investigation with the population concerned. I recognise the possibility that there may not be a sufficient challenge or a satisfactory professional climate in the work and associations of the manufacturing plant, but even so, I think it preferable to the location in the Company headquarters unless some adequate outlet for one's medical efforts can be found in London.

With the foregoing tentative comment, I conclude for the present.

With best regards.

Sincerely,

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Enclosure

RAK:ss

Robert A. Kehoe, M.D.