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July 26, 1956

Dr. Robert E. Eckardt, Director
Medical Research Division
Esso Research and Engineering Company
P.O. Box 121
Linden, New Jersey

Dear Doctor Eckardt:

Time has had wings since I received your letter of June 8th, concerning the organic lead compound trimethylethyl lead, for I have been trying to clear away a mountain of unfinished work including correspondence, so as to get away for a vacation. Now that June and July, alike, have flown, with the exception of a few days of the latter, I feel that I must not wait longer to find a suitable date for a meeting with you, but must write to you instead. Otherwise, I shall be responsible for an undue delay in dealing with this matter. I am sorry now that I did not write to you about this promptly.

Since our initial conversation, I have consulted a few responsible persons in Ethyl Corporation, and I am in position to give you the essential toxicological information and to express my views on the problem of the use of this material. I had no reservation at any time in furnishing you with the toxicological facts, but I could hardly talk to you without considering with you the hygienic aspects of the entire situation. I hesitated to go into the latter without consulting my associates in Ethyl Corporation, since as Ethyl's Medical Director I could not, in such a matter, fail to speak to some extent for the Corporation. As it is, I am informing Mr. Scales of the Detroit Laboratory and Mr. Murdock of the Sales Department, by confidential copies of this letter, of what I say, since I must be sure that there is no ambiguity in my words or meaning.

First, with reference to the essential facts on the toxicological behavior of trimethylethyl lead:

- (1) This compound, somewhat more dense than tetraethyl lead, and in round numbers about ten times as volatile, has much the same toxicity and mode of action as does tetraethyl lead, being slightly more toxic when administered by mouth, considerably less toxic (apparently less readily absorbed) when applied upon the skin, and somewhat more toxic (gram for gram of Pb) when inhaled as a vapor. The concentration of these compounds in air, which is lethal for rabbits exposed thereto for one hour, is of the order of 1 to 5 mg. expressed as Pb, per liter of air.

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- (2) The foregoing minor differences in the toxicity of these two compounds have little practical significance in promoting any real differences in the long-term hazards of occupational exposure to them, since the fact of their absorption through the skin and after inhalation is the really important consideration. Under these circumstances the hazard depends as much upon the duration of the exposure as upon its severity.
- (3) The distribution of this compound within the tissues of animals to which it has been administered, both initially and subsequently, is of the same type as that of tetraethyl lead, as judged not by any considerable number of direct observations made on the behavior of trimethylethyl lead, but rather from a comparison of the behavior of tetraethyl and tetramethyl lead, these two compounds, only, having been investigated extensively.

Second, the potential hazard created by the substitution of trimethylethyl for tetraethyl lead must be considered in two relationships:

I. The hazards of manufacture

Quite apart from the problem which may be presented by the greater chemical instability of trimethylethyl lead as compared with tetraethyl lead (this is assumed to be the case, and while the information available to me on this matter is inadequate, it is a problem to be reckoned with seriously from the hygienic aspect), the real problem lies in the greater volatility of this lead compound as compared with that of tetraethyl lead.

The lack of an appreciable incidence of tetraethyl lead poisoning in association with the manufacture of tetraethyl lead as it has been carried out by carefully trained, highly capable and well supervised people in the U.S.A., Great Britain and France (and earlier in Germany) should not delude anyone into the belief that this is not a highly dangerous manufacturing industry. Something near to perfect performance in the arts of production is required to maintain these operations in safety, while the medical and hygienic regimen required to secure and portray the safety of the manufacturing personnel is one of the most intensive and sustained efforts that is known to industry outside of the area of atomic energy.

It is difficult to anticipate all of the problems that would be presented by a several-fold increase in the volatility of the product to be manufactured. There is little doubt that the difficulties could be overcome in the manufacturing operations, but a step-wise development of the process, on a relatively small scale, would be necessary to the achievement of safe methods of manufacture. It would be utterly foolhardy to take use of the present manufacturing facilities for the large-scale manufacture of trimethylethyl lead.

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II. The hazards of the distribution and use of the product

The commercial distribution of gasoline containing tetraethyl lead within the prescribed limits of concentration has been shown to be safe from the aspect of the exposure of gasoline handlers to tetraethyl lead (excluding the special problem of tank cleaning). The factors responsible for this safety, as demonstrated experimentally prior to the extensive use of leaded gasoline, and confirmed by experience, are those of (1) the dilution of tetraethyl lead by gasoline to such an extent that its absorption through the skin is hindered to the practical vanishing point; and (2) the suppression of a significant amount of vaporization of tetraethyl lead from gasoline in ^{open} containers by its dilution in a solvent (gasoline) of relatively high vapor pressure (the application of Raoult's Law to this system foretells the facts demonstrated by experiment). It thus happens that hundreds of thousands of people in the petroleum industry handle present-day leaded gasoline without absorbing a practically significant quantity of lead. They do, however, absorb some lead, the quantity being insignificant as compared with other sources, while the total level of absorption is insufficient to result in a measurable accumulation in the body in a lifetime.

The margin of safety in the above situation is appreciable but difficult to measure. I cannot contemplate the effect of a ten-fold increase in the volatility of the lead compound in commercial gasoline without great concern, for despite an anticipatory approach to this problem by experimental means, the final test of the safety of the procedure will have to be that of practical experience. It is my considered opinion that it would be unwise to incur the risk of experience in establishing the facts in this matter. Not only would this be costly in terms of experimental work of various kinds, but it may well turn out to be unsafe. Back-tracking would be a difficult and costly procedure, especially from the aspect of public understanding.

I trust that this will serve to convey both the facts, which are very simple, and my opinions, which, I hope, are equally simple to follow. If I raise questions that require further examination I shall be glad to discuss them with you.

Sincerely yours,

RAK:vr

Robert A. Minkard, F.D.

cc - Mr. R. K. Scales
Mr. M. P. Murdock

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