

THE ASSOCIATED ETHYL COMPANY LIMITED

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DR. P. S. I. BARRY
Chief Medical Officer

OUR REF.
YOUR REF.

19th May, 1960.

Dear Dr. Kehoe,

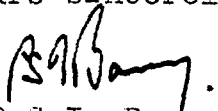
I enclose copy of a letter that I wrote recently to Professor Sir Charles Dodds on the subject of the toxicity of tetramethyl lead.

I appreciate that you are well aware of the work done by the M.R.C. Toxicology Research Unit at Carshalton, Surrey, on the mechanism of the toxicity of tetraethyl lead which was published by Miss Cremer in the British Journal of Industrial Medicine in July, 1959, and feel sure that you would be interested in the work that they are at present undertaking in connection with tetramethyl lead. I hope that they will be able to undertake a series of inhalation experiments to determine environmental L.D. 50 levels for both tetraethyl and tetramethyl lead, and so provide us with comparative figures of levels of toxicity for these two compounds on an environmental basis.

I was very pleased to learn from Mr. Bevan that you will be paying a visit to this country and to Europe in June for one month prior to the 13th International Congress in New York, and look forward to meeting you and discussing our problems, particularly those relating to tetramethyl lead.

With kind regards,

Yours sincerely,


(P.S.I. Barry)

Dr. Robert A. Kehoe,
M.D.,
The Kettering Laboratory,
College of Medicine - Eden Avenue,
Cincinnati, 19, Ohio.

Enc.

PSIB/pby
c.c. The Managing Director

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6th May, 1960.

Dear Sir Charles,

During the course of our lunch meeting on March 8th, I promised to keep you informed on the progress of work being undertaken by the M.R.C. Toxicology Research Unit at Carshalton, Surrey, on the toxicity of tetramethyl lead.

I visited the Unit on Wednesday last, May 4th, and the work done so far indicates that when tetramethyl lead is administered to rats by the oral route, its toxicity is of the order of 1/7th that of tetraethyl lead on a weight-for-weight basis. The symptoms produced at toxic levels of tetramethyl lead and tetraethyl lead are precisely similar but there is a longer period of delay between the administration of the material and the onset of symptoms, probably due to a slower rate of conversion from the tetra- to the tri- form, in the case of tetramethyl lead. The intravenous administration of tetramethyl lead to rats, even in large doses, produced no symptoms.

The pattern of response in the work done so far would appear in the case of tetramethyl lead to follow that of tetraethyl lead where it has been shown, in a paper published by Miss J. Cremer in the British Journal of Industrial Medicine, that the triethyl lead radicle is the toxic agent and that tetraethyl lead, in "in vitro" experimental-work, is non-toxic.

The L.D. 50 figures for rats, following the oral administration of methyl and ethyl lead groups, are represented as follows: -

L.D. 50 for rats (mg.kg.)

	Tetra	Tri
methyl	105	25 - 30
ethyl	15	11

I have suggested to the Director of the Unit, Dr. Barnes, the possibility of his undertaking a series of animal inhalation studies, using the methyl and ethyl lead groups, with a view to determining environmental L.D. 50 levels, as I feel that this could be of considerable practical interest, particularly in terms of the relative toxicities of these groups. Dr. Barnes is interested in the suggestion but the laboratories of his toxicology unit are not normally equipped to undertake such work. However, he has agreed to investigate means by which this could be done, if not at Carshalton, perhaps at Porton where they are fully equipped for such work. I shall keep you informed as further developments become apparent.

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I sincerely hope that you will find an opportunity to pay us a visit at Ellesmere Port this year. During our luncheon meeting on March 8th I think you indicated that some time during June would be convenient to you but that you would confirm this at a later date. We would be very pleased indeed to have an opportunity of seeing you up here and of discussing our various problems.

With kind regards,

Yours sincerely,

(P.S.I. Barry)

Professor Sir Charles Dodds,
The Courtsauld Institute of Biochemistry,
The Middlesex Hospital,
LONDON, E.1.