

October 15, 1957

AIR MAIL

Dr. Philip Boyd
The Associated Ethyl Company, Ltd.
20 Berkeley Square
London, W.1., England

Dear Philip:

Your last two letters, August 9th and July 30th, came to my office when I was on vacation in Colorado, and the two dated July 25th came just as I was leaving for Salt Lake City, where I spent three days at work (of a sort) just prior to the serious job of vacationing. Since my return to my office on September 3rd, it has been quite impossible for me to do more than keep my head above the flood level of the day's work, so that my correspondence has suffered almost complete eclipse. I am doubly sorry - that is, on both professional and personal grounds, - that this has been the case, and an additional weight of guilt hangs over me for not replying earlier to a letter of yours of May 28, with its generous supply of information. I can only ask for your forbearance for appearing to be lacking in both courtesy, and regard for you. I am sure you know that the appearance is not the fact. I believe I shall be able to do better in the future, for things are looking a bit more hopeful, but I may be unduly optimistic. Certainly, there are still many things waiting to be done.

I shall begin with your last letter, and work backward to the first. Let me say, however, before beginning any kind of response, that you must not allow yourself to doubt that I would respond promptly to any urgent call from you. Thus far the problems which you have brought to my attention were not especially urgent, or so it seemed to me, and I could set them aside for consideration after more urgent matters had been disposed of. As you know the day of reckoning tends to extend itself farther and farther into the future, when one is pressed for time, and while I have not done well, I have not, I hope, failed entirely to give things a reasonable priority. If you must have a prompt reply from me, or some sort of prompt action, do not hesitate to tell me. I can always cable, and I don't regard anything I can do for you, or for Roy Bevan, or indeed for Associated Ethyl, as burdensome. As you know, however, close friends and associates are likely to suffer somewhat in these matters, by virtue of their known capacity for understanding and tolerance.

With reference to the problem of buried sludge, we have indeed

Dr. Philip Boyd -(2)-

October 15, 1957

done a great deal of experimental work. I could put together a report that would seem to be impressive by giving the extensive data which we possess on the concentration of TEL and its degradation products (which we separated into triethyl, diethyl, monoethyl and the inorganic fractions) in sludge. Unfortunately, none of the data appear to have meaning in relation to the practical problem at issue, and I have not prepared any report at all. The difficulties, which will confront you as well, if you undertake to investigate this situation, are in the following categories:- (1) it is difficult to obtain representative samples of buried sludge; one should know the characteristics of the sludge before its burial so as to have a basis for comparison afterward; the initial characteristics of the sludge are altered by drainage, seepage into the surrounding soil, and settling, and, in all probability by several other factors; the organic lead content of most sludges is low and therefore it is difficult to find highly significant differences before and after burial. In short, having failed to learn anything very significant about this matter by the seemingly simple method of sampling and analysing sludges that have been buried for various fairly long periods, we have decided that the only way we could tackle the problem is by setting up an experiment in which most of the variables would be under control. This has not been done because other problems offered more promise of being investigated productively. All I can say, that has any practical value, is that the risk associated with digging into buried sludge, after a period of years, from the aspect of volatile lead compounds, is considerably less than I would have anticipated. This is the case, however, in many, if not most instances, because the sludge when removed and buried was not very high in its organic lead content. (We suspect that the dangerous situation in American practice number less than ten per cent). What would happen if the sludge were really high in its organic lead content, and if it were to be confined in a part of the earth that afforded little opportunity for drainage, or seepage, is another matter. I shall be interested to know how you approach the problem, if you decide to investigate it, and also what you are able to learn. As my remarks indicate, I am not very sanguine as to the outcome of field tests of this type.

Now as to the manganese anti-knock compound, this product is a complex organo-metallic compound - methyl cyclopentadienyl manganese tricarbonyl. Such compounds, so far as toxicological literature is concerned, are unknown, and the only information available is the preliminary information which we had obtained, and that which was obtained by Carbon and Carbide fairly recently when they looked at a similar compound of manganese for use, I believe, for some other purpose. (Incidentally, there is some

KE 0010180

Dr. Philip Boyd -(3)- October 15, 1957

problem here with respect to patent rights, but I do not know enough about the matter to enable me to say more).

Since this compound is one of a group of organo-metallic compounds, that has been under separate investigation, (research for a satisfactory anti knock compound) for some years, it (and practically all comparable or analogous compounds) is a laboratory curiosity and it would be practically unthinkable that there would be any toxicological information on it. As you will realize, through a general knowledge of my views on such matters, we began to examine this compound, toxicologically, when certain preliminary technical experiments indicated that it had some promise. The first step, which can be undertaken only when there is reason for it in terms of some program of continuing technical investigation, is that of a screening process, whereby the avenues of absorption, the acute manifestations of toxicity, and the pathologic pattern, are investigated. This compound, and a related solid compound, gave such highly unusual promise of technical usefulness that the usual steps in the technical development have been short circuited and expedited. Accordingly, about all we have had time to find out about the toxicology are the results of the preliminary screening. This is, however, much the most dramatic discovery in the anti-knock field since TEL, and therefore we have embarked upon an extensive, and intensive, investigation, which is very likely to achieve the scope and significance of the work on TEL, including the extent and significance of the manganese in the exhaust. Reports will be available from time to time, and these will be sent to you.

For the present our work demonstrates only the order of magnitude of the toxicity of the compound. I shall not bother with the details, since a report on these observations, and on longer-term investigations, will be out fairly soon. The compound is absorbed through the skin; it is, of course, toxic when swallowed, and its vapor can be absorbed, of course, via the respiratory tract. The lethal dosages and concentrations are of the order (somewhat less) of tetraethyl lead. All we can say at present, from both experiment and experience, is that the material must be handled as tetraethyl lead is handled, and that if such precautions are taken faithfully, no untoward effect is to be expected.

We know nothing at present of the characteristics of the distribution of the material in the body, or of its metabolism in the body. (This is why preliminary toxicological data are of little value). Analytical procedures are being developed to cope with this part of the experimental program. Experiments on the absorption of the compound out of gasoline at different levels of dilution are under way. In short, we are pursuing as rapidly as we can, the facts with respect to the hazards of manufacture and handling, the potential hazards related to gasoline containing the compound, and the potential hazard of the appearance of inorganic manganese (the nature and degree

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001018f

Dr. Philip Boyd -(4)-

October 15, 1957

of dispersion of the compound in the exhaust is being investigated in Detroit) in the air breathed by men. We are, in fact, presented with a large series of problems on which one could speculate at length, but which must be answered in a fairly definite manner. This whole matter promises to telescope into significant form within a small fraction of the time required to exploit and develop TEL, and therefore, we must make haste correspondingly.

The development of this compound and the potentialities for its use, within the next two years, in addition to TEL, in automobile fuel, finishes, I believe, and certainly holds in abeyance, for the present, any consideration of the fourth milliliter of TEL. As to the toxicity of the combination of lead and manganese in the exhaust gas, (both in inorganic form) all I am prepared to say is that manganese compounds appear to be much less dangerous-gram for gram - than lead. I should suspect that the two would not be additive in effect. Manganese is wide spread in nature, and is relatively high in its representation in the vegetation, and in the animal and human body. We shall have to learn the facts on a fairly broad base, but I look with considerably less concern on some increase in our exposure to, and absorption of, manganese, than I do on a further increase of any appreciable proportions in our exposure to lead. I should say also, that I look with great interest upon our opportunity to learn about manganese, what we now know about lead - the details of its occurrence in nature, its distribution in the animal organism, its metabolism, and its total physiological significance, especially for man, so far as we have the wit to ascertain such facts.

Finally, do not expect to have much of the information on this compound for some time, but when it becomes available, in reasonably satisfactory form, I shall forward it to you. Meantime, if any specific questions arise let me have them. I'll answer as well as our information will permit. There is, of course, no secret on the toxicological side. This compound looks like the answer to the investigator's prayer in the anti-knock field, and if it fulfills its promise, all we can learn must be made widely available, not only to the industries involved, but in the literature.

I go now to the more troublesome matter of our medical consultants in various parts of the world, and I am more than grateful to you for the information which you have given me, and the suggestions which you have made. Let me say first that I cannot follow one of your suggestions, despite its apparent reasonableness and simplicity. I have been instructed in a definite manner by

KE 0010182

October 15, 1957

Fred Warne, (Ethyl's Chief counsel), who is without competitive prejudice, I believe, that I must not, under any circumstances, make any arrangement with you whereby you look after anything that may be regarded as Ethyl's operating affairs, or I look after corresponding activities of Associated Ethyl in the competitive field. You and I can consult freely on matters of hygienic policy, and exchange information on medical matters and modes of procedure, but we must not mix the actual field operations of the two organizations. The issue, from the aspect of American law is quite clear to Fred, and he has instructed me, (not just merely advised me) accordingly. I have no choice but to comply. There are aspects of the situation that strike me as utterly unrealistic, but I have no choice.

I have handled this general matter as well and as simply as I can, by advising the sales representatives of Ethyl for the several areas (Nick Carter, Ed McDonald and Bill Trelease) and the head people in Ethyl's Sales Department (Bayard Browne, Hank Ball and Julian Fray) of my wishes in the matter of local consultants. In a fairly long and definite conference with them, I have made it clear that I will not have medical representatives of Ethyl placed in a non-professional, competitive position. We are to use the consultants that are on the job whenever this is feasible and desirable, as judged by me. The men are to negotiate with the physicians locally, according to my instructions to them, and are to provide me with information and an expression of their best judgment, the actual appointment to be made by me or on my authority. Two things however, are imperative - (1) Ethyl must make its own financial arrangements, not in disregard of yours, rather, so far as possible, like yours, and without prejudice to the over all economic and professional relationship of the physician in question; and (2) the working relationship (instructions, reports, etc,) between consultants and Ethyl's Medical Department, must be direct and not through you. These features of my instruction make it impossible for me to agree to your otherwise reasonable, and sensible suggestions, for mutual assistance. I know full well that we are making a difficult situation worse by means of these oblique approaches, but I can't help that at the moment. I shall let you know, in due course, what we have done in the areas into which Ethyl's business activities have caused us to develop consultant relationships.

I agree that we should, if it is possible, arrange for some discussion of these matters between Associated and Ethyl personnel, but I have no hope of being able to arrange this in the immediate or near future. I shall keep my eyes open for a favorable opportunity. I must say, that I have practically no hope of being able to deal effectively with the DuPont group in this matter. I may be wrong, and if an opportunity presents itself for discussion or action, I shall take full advantage of it. It is possible that I can do more about this after I retire from Ethyl's Medical Directorship, at the end of 1958, than I can at present. We shall see. I am certainly stymied at present. Meanwhile, I am working as consistently as possible toward a situation in which one capable physician will carry out the medical service on behalf of the people

October 15, 1957

at hazard in a particular area or country, regardless of the supplier of the product. This is the fundamental thing to be achieved, whereas the mechanism of the relationship otherwise, with respect to compensation and professional reporting, despite its necessity, is of secondary importance. If we can have that kind of professional responsibility and capability, we are in a good position, but if we cannot have that we have nothing worthy of any concern on your part or mine.

This brings me to the question of Dr. Akatsuka. I have looked into this matter as well as I know how, (through a colleague of his, whom I trust; through enquiries instituted by Nick Carter, who, despite his primary interest in Ethyl's advantage, is an honest man and an astute observer; and through direct correspondence with Dr. Akatsuka). With reference to the latter procedure, I raised specific questions with Dr. Akatsuka concerning both his conduct and his motivation. I was not more blunt than it seemed necessary to be, but I stated my views and laid down my requirements. The reaction to my letter, as represented in Dr. Akatsuka's reply to me and his subsequent discussion with Carter, which was reported to me faithfully, I believe, was reassuring, and it appeared to me to be what I should have expected if my Japanese colleague was right in his judgment. (I refer here to Dr. Susuma Harashima, Professor of Preventive Medicine (Head of Dept) and Public Health in the School of Medicine, Keio University Tokyo, with whom I talked at length, in Geneva, in March)

It is difficult to gauge the validity and significance of Dr. Akatsuka's actions and the things that are said about him by others. There is no question about certain quirks of his personality, which make it difficult for me to appraise his motivation. There are characteristics of the general situation, in Japan, however, which are so different (or so it seems) from those with which you and I have to deal within our own countries, as to make me uncertain as to the merits or demerits of his behavior. It seems to me however, despite these uncertainties, that he is the best informed man in Japan on the subject of tetraethyl lead, and the manner of getting it into gasoline; that he is doing a good job, in fact, of supervising and safeguarding the men who are engaged in mixing operations. These are the things in his favor, and I hesitate to do anything that might react to compromise these benefits. Against these features of the situation is the man's clear determination to be the supreme authority in the handling of this problem, and not to share his knowledge of the matter with anyone, and his general tendency to acquire arbitrary and dictatorial powers. It appears, in addition, that he is not unmindful of his economic advantage. Generally speaking, I would agree with you completely that Dr. Akatsuka's personal qualities of ambition, authoritarianism and self-interest, are reprehensible and undesirable. Certainly as human characteristics they are in the undesirable category. On the other hand I cannot tell how far these apparent characteristics go, or what they signify. It seems likely that Japan will go her own way, in the not too distant future, in the matter of the manufacture, distribution and use of tetraethyl lead. When that time comes, Dr. Akatsuka's knowledge of the subject may prove to be of the

0010184

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Dr. Philip Boyd - (7) - October 15, 1957

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greatest usefulness, and even his capacity to dictate (not to different in principle, but different, I hope, in method, from my own efforts) may be valuable. I cannot be sure just where we are, and I cannot advise you what to do, with any feeling of competence. My own attitude, however, at this time, is to let matters take their course, while I maintain as close contact with the situation, at this distance, as may be possible.

I have not commented on all of the aspects of the matters referred to in your letters concerning Japan and Dr. Akatsuka, or other places and other doctors. As I indicated above, I shall let you know what we do in the matter of consultants in the areas in which we are both concerned. I should tell you that the matter of the washing out of drums, with gasoline, has been discussed. We do not consider the washing procedure to be mandatory, and indeed, we consider that the hazard presented by a drum which contains residual gasoline in appreciable quantity, is a serious one in transportation. If such gasoline is unduly high in its lead content, the hazard is thereby greatly increased. Our people in the field will not make an issue of this. The points made on the matter in the DuPont letter (attached to your's of July 30th) were those originally stressed in connection with the procedure of washing. Their validity at present is certainly open to question. I agree however, that other things in this letter were more significant to us than is this matter of the gasoline wash. The entire flavor of the letter is unsatisfactory to me, and I wonder, of course, whether this arises out of the attitude of DuPont or that of Dr. Akatsuka, or a synthesis of both. I agree with you that these are not matters in which Dr. Akatsuka should be concerned primarily, but I cannot contend too strongly, in that direction, without knowing who is responsible for the situation, in view of the fact, with which you are familiar. I am sure, that I have been deeply involved in all such matters myself, and only in recent years have I turned them over essentially (not entirely) to Van Fleck, and then to his successor Henry Ball. Even now, I am always consulted on these matters, as I feel sure you are also, in Associated councils.

With respect to one additional matter - that of the general investigation of background problems, the situation may be altered somewhat by the invasion of management into the field. This may, or may not interest you and your group at this time. From the aspect of lead there are many things that can be done. As I have indicated previously, the practical problem that appears to me of greatest significance, is that of the comparative situation in Britain with respect to the occurrence of lead in food and beverages. This is not an exciting problem and it may not have a sufficient appeal for you. There are several ways of attack upon it, however, and if you should decide to go at it, I could make some suggestions. I am convinced that someone will have to do this sometime, and I feel sure that it is worth doing. Another problem of similar

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0010185

Philip Boyd -(8)-

October 15, 1957

character, of course, is the distribution of lead in the atmosphere of Great Britain. This too, will have to be done some day. If either of these general problems were to be attacked, the facts concerning both lead and manganese, as well as certain other metals, could be obtained at the same time with economy. It has always seemed to me to be an extravagance to go to the great trouble and effort of obtaining suitable samples of materials representative of the general human environment, and then to analyse them for but one element. Particularly, is this true when such methods of analysis as the spectrographic have fairly wide application to a number of elements simultaneously.

So much for matters now in correspondence. We heard from you indirectly when our youngest godchild returned from England recently, and reported on your efforts as a host on her behalf. Apparently her summer was a great success, and she was delighted with your hospitality. It was good of you to give her a good time, and I am sure that you enjoyed it. She has a great deal of both charm and substance, and is far and away my favourite among the Foshay clan.

And now this letter has gone on for a very long time, and has made some amends, I hope, for my long silence. It is time to get on to other things. I'd appreciate it greatly if you would convey my greetings to Ray Bevan, Beery Noble, Charlie Rizzo-Gill, and others of my very good friends at 20 Berkeley Square. It seems but a short time since I visited you there, and yet I recognize in terms of the calendar that many months have sped along since then. Let me hear from you when the spirit moves and time permits, regardless of the occasion. And again, let me urge you not to spare me from your messages or questions, lest I should be overburdened by them. I may not respond promptly, but I shall surely.

With best regards,

Sincerely yours,

Robert A. Kehoe, M.D.

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