September 17, 1958

Dr. Lamson Blaney
Medical Director
Sun Oil Company
Philadelphia 3, Pennsylvania

Dear Lamson:

I am sorry not to be able to provide you with a detailed report of our observations, to date, on Ethyl Corporation's AK-33X. We have range finding information and we are procuring data that will serve to define in reasonably precise terms the actual hazards, with special criteria for the avoidance of hazard. In such work, however, time is the important factor that cannot be short-cut, and there is no way by which acute effects can be used in the interpretation or prediction of chronic effects. Meanwhile we are surrounding the product with precautions which may turn out to be somewhat excessive, but which, in my present judgment, are not. These will permit its development in application without any significant risk to anyone.

As the physician directly responsible to Ethyl Corporation, I initiated work in this Laboratory on this material over a year ago. The following general facts are available, and since precise figures at this point are redundant and may be misleading, I am giving the facts to you in general terms. Reports will be available a bit later, when they are ready for publication.

(a) The immediate toxicity of the manganese compound, which is roughly comparable in its general chemical structure to the organic compounds of other metals, is of the same general order of magnitude as the lead alkyls.

(b) The material is capable of being absorbed through the skin, apparently not as readily as tetraethyl lead, but at a sufficient rate to induce acute and lethal intoxication.

(c) It is sufficiently volatile at ordinary temperatures to pose the problem of inhalation of its vapor, when it is handled in undiluted form or in moderate to high concentration in an organic solvent.

(The toxicity of the vapor has not been worked out, as yet, in terms of a series of time x concentration equations which define conditions required to induce death, for the emphasis, in our experimental work, has been

put on the effect of low concentration in an effort to determine rough limits of safe concentration, in relation to manufacture and handling, at the earliest possible time.)

(d) The absorption of the material through the skin is greatly retarded by its dilution in petroleum solvents, and the preliminary data indicate that it becomes insignificant when its concentration in gasoline approaches, but is several times the level anticipated in its commercial use.

Our purpose, in our experimentation, has not been that of obtaining information for publication or dissemination, although that will come in due course. Rather we have attempted to learn, as rapidly as possible, the facts which will enable us to throw proper safeguards around the experimental and developmental procedures, at first, and to develop criteria for satisfactory working conditions, with respect to atmospheric concentrations, and procedures for personal protection when such may be required, including metabolic and excretory data. In such a program, precise data in relation to acute intoxication are of very little value, except in defining the modes of absorption and the location and the nature of the toxic effect. For this reason we have little to give out at this time beyond the general statements made above. With these items of information in hand, we have advised Ethyl Corporation and those engaged in experimental use of the product that the material resembles tetraethyl lead in its behavior and in the hazards which it provides, and that the faithful application of the precautions applied in the handling of tetraethyl lead will insure their safety in the handling of this material. I have carefully avoided giving out fragmentary data on the immediate toxicity of the compound, since these would lead to unwarranted comparison of the degree of hazard, and result in a variety of attitudes toward the precautions which we have advised. Having been through this in the case of tetraethyl lead, I am not prepared to repeat the experience. In this relationship, let me emphasize the fact that the real problem here lies in the meagerness of our understanding of the behavior of manganese. There are other problems, of course, in relation to other parts of the molecule and to the whole molecule. In the long run, however, the thing that must be investigated thoroughly is the metabolism of manganese in the animal organism, since the discharge of an inorganic manganese compound into the atmosphere from the exhausts of automobiles may well be the most significant of all of the hygienic problems. I am not even slightly apprehensive about the problems of manufacture and handling, if we can maintain the regimen that has served in the manufacture and handling of tetraethyl lead. I am not especially apprehensive about manganese in the air, but, on the other hand, this poses a question which must be answered. We have, therefore, a comprehensive investigation ahead of us, and we are getting at these essential matters as promptly as possible without wasting our time, now, on the precise figures (LD 50's and the like) which would describe the immediate toxicity of the compound following various methods of administration. These will be required to make a complete story and will be filled in. But they will not help us much, at present, in drawing

up precise specifications for safe occupational practice.

I have gone to some length to explain this situation, for I should not wish to convey the idea, by indirection, that there is anything of a mysterious or covert nature in it.

Sincerely yours,

Robert A. Kehoe, M.D.

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