

American Petroleum Institute
(THE METABOLISM OF LEAD)

N13360

RE 0012394

March 1

Robert E. Eckardt, M.D.
c/o American Petroleum Institute
1291 Avenue of the Americas
New York, New York 10020

Dear Doctor Eckardt:

I am sending herewith a revised copy of the prop
to the International Lead Zinc Organization for
as may be taken in connection with this project
American Petroleum Institute. Pages 1 and 2 are
(so as to keep this portion of the record as it
August 1965), while pages 3 and 4 have been alte
bring matters up to date.

I trust that this will be satisfactory for your

Sincere

Robert

RAK:wp

enclosure

KE 0012395

On October 3, 1962, the general experimental procedure and together with the details of a specific experiment to be were described in detail. Further proposals, relating to of the work, were made on September 4, 1963 and on September work has gone on in essential accordance with the purposes described in these proposals, and is to be continued in similar lines indicated herein.

The immediate goal of the experimental work in 1965 was through human experience, the maximum concentration of in and absorbable (i.e., pulmonary absorption, exclusively) the ambient atmosphere to which normal, healthy, human subjects subjected, continuously and for indefinitely prolonged periods incurring the potential risk of a demonstrable degree of in their bodily tissues.

The experimental principle involved the exposure of two parallel respiratory chambers, to air containing lead (as of Pb, as lead sesquioxide, per cubic meter) dispersed in (ranging in diameter from less than 0.01 to 0.18 microns of 0.05 microns), on an intermittent schedule of increase per day every other day for approximately 16 weeks, i.e. 6 hours per day every other day for approximately 16 weeks; and so on to 31.5, 42.0 hours, etc.) until the effect became evident through a slight (statistically demonstrable) output or concentration of lead in the urine, presumably (experiments) without demonstrable increase in the concentration of blood, of the subjects.

During 1965, these observations have continued as scheduled adaptation of the periods of exposure to the tolerance of disruptions of their daily lives. That is, when the schedule of requiring the subjects to spend more than 12 hours per (on alternate days) it became necessary to shift to daily. Obviously, also, the continuation of the family life of at least, one day per week of freedom from exposure. The schedule, involving the proper number of hours of exposure into equivalent periods on six of the seven days of each (August 1965), one of the subjects (N.K.) is spending 63

6 days per week, with due regard for the comfort of the subjects. If then no response shall have been obtained, the concentration of lead in the chamber will be increased by a series of incremental increases in the duration of exposure, beginning at a level of intensity (time x concentration) which will duplicate that of previous steps. It will be necessary to obtain a response, and such response must be graduated through at least three levels in excess of the previous to provide data for extrapolation to the effect of a continuous exposure (24 hours per day on 7 days per week). According to the schedule expected to continue through the entire year 1965.

It is conceivable that the experimental regimen might be shortened the time required to obtain definitive results. The factors being doing are under consideration at present, and the possibility will be explored critically at the end of this calendar year. The risk, however, in any radical alteration of the schedule of the experiment, in that too sharp an increase in the concentration of lead could cause an excessive response, and threaten, thereby, the health of the subjects. It was for this reason that the initial concentration of lead in the chamber was set at 10 micrograms per liter, which could be counted on (from indirect but satisfactory data) to yield negative results at first, with the possibility of obtaining a positive response as the time factor progresses.

With the present facts and anticipations in mind, the schedule for the program in 1966 is expected to be similar to that of 1965. It may be affected, since it seems unnecessary, in 1966 to analyze duplicate samples of the food of the subjects. The similarity between the lead in the food, day by day, with the results of the experiment is so satisfactory as to enable the former item to be omitted, apparently without introducing an error that is significant. Further statistical work will be necessary to establish this in this regard with certainty, and this feature will be explored critically at the end of the current year (1965).

RE 0012

First, with reference to the experimental results now said that one of the subjects (N.K.) completed the des 16 weeks, to air containing 10 micrograms of lead (und described in detail previously) on February 20, 1966. reasons explained previously, will not reach this poin being no significant evidence of a response to this ex (approximately half of each 24-hour period), it is evi of lead in the chamber will have to be increased, and have to go on for somewhat more than a full year from in order to provide the points on a curve from which a made to the effects (on the urinary excretion of lead of the blood) of exposure for 24 hours per day every d experimental regimen can be inaugurated is somewhat un because of the uncertainty of the willingness of the t continue for an additional period of eighteen or more matter is being worked out. (It will be considerably proceed with the same subjects, than to go through the on two new subjects, with their period of indoctrinati There is hope that this can be avoided.)

Second, it is now somewhat uncertain, for several reas of funds, whether the renewal of the application to th be approved and activated. The expectation is that th the expenditure of funds is being scrutinized so as to the experimental program if this should not come about the expectation that a share of the expenditures (as i assumed by the American Petroleum Institute, a new bud submitted at this time, together with a statement of t funds. Curtailment or some degree of accelleration of affected in accordance with the outcome of the financi way. (In this connection, the economy that may be rea eliminating the analyses of food and beverages, has be Recent consideration of the direct usefulness of the i the food of the country, have convinced us that these abandoned unless it becomes necessary to do so, for th

The following budget is recommended for 1966, on the b made in 1964 and 1965, and of those now visualized:

For personnel and services (direct and indirect costs)
For special reagents, supplies, allowances for food, e
Overhead (proportional share of cost of operating the
Laboratory)

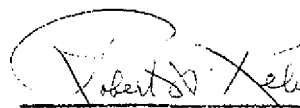
Total

KE 001239

International Lead Zinc Research Organization
American Petroleum Institute
U.S. Public Health Service

Total

Should the Public Health Service grant be discontinued,
be made to stay within the limits of \$100,000.


Robert A. Kehoe,
Kettering Labora

Date: March 11, 1966

KE 001238