

PROPOSAL TO INTERNATIONAL LEAD ZINC ORGANIZATION FOR THE CONTINUATION,
THROUGH THE YEAR 1968, OF THE FINANCIAL SUPPORT OF THE PROGRAM OF RESEARCH
IN THE KETTERING LABORATORY, IN THE DEPARTMENT OF ENVIRONMENTAL HEALTH
OF THE COLLEGE OF MEDICINE OF THE UNIVERSITY OF CINCINNATI, ON THE PROJECT
"HUMAN EXPOSURE TO PARTICULATE LEAD COMPOUNDS IN THE AIR UNDER EXPERIMENTAL CONDITIONS"

In the proposal dated August 18, 1966, the experimental program for 1967 was outlined. Since that time and up to the present date, July 15, 1967, this program has been pursued diligently. The experiment as described (August 18, 1966) has been completed and the results have been reported (July 1966 and February 1967). Another experiment, which followed logically from the results obtained previously, was outlined for initiation in early October 1966, and was expected to continue into August of 1968. (This experiment has been described in the progress report and need not be detailed here.) In short, in view of the essentially negative response of the experimental subjects to respiratory exposure to air containing 10 micrograms of lead per cubic meter, the level of concentration of lead in the new experiment has been increased to 20 micrograms per cubic meter.

The two subjects were kept on the same experimental regimen until June 19, 1967, at which time they had completed a first period of 20 weeks of exposure to air containing 20 micrograms of lead per cubic meter (which had extended from October 10, 1966 through February 19, 1967), and a second period of 16 weeks (which had extended from February 20, 1967 through June 18, 1967). During these two periods, the time spent by each subject in the respiratory chamber amounted to 21 hours per week (first period) and 31.5 hours per week (second period).

Early in June, just before the Commencement exercises of the University of Cincinnati, one of the experimental subjects reported that, having been assured of being awarded his Master of Arts Degree at the Commencement, he had been granted a scholarship at Yale University, for the continuation of his studies, and that his faculty advisor had urged him to accept it, if he could possibly do so.

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advantage of this somewhat unexpected opportunity to advance his career. It was, of course, a situation that had to be faced, and could hardly be dealt with in any other manner than to the advantage of this graduate student. The scholarship had been granted for a full year beginning September first of this year.

In order to obtain as much benefit as possible from Subject H.R., and from the comparative behavior of the two subjects, during the brief period remaining, the second period of the experiment (indicated above) was terminated at the end of 16 weeks, and the third period was initiated on June 19, 1967. Both subjects were dealt with in this manner, except that one of them, Subject S.S. (who would continue on into the next year), was shifted to 42 hours of exposure per week, while the other, Subject H.R., changed to the rate of 63 hours of exposure per week. This was done because Subject H.R. would remain but for 10 weeks, and the best use of his time and effort during this period appeared to be that of finding out whether the severity of the exposure at the level of 20 micrograms per cubic meter for 63 hours per week would be such as to induce any excretory response in so short a time as 10 weeks. Should this turn out to be the case, a means might well be provided of expediting the course of the experiment involving the other subject. (Or perhaps it might be best to terminate the experiment at 20 micrograms per cubic meter and go to 25 or 30 micrograms per cubic meter. The speeding up of this experiment should result in information that will determine whether a further experiment is required, and at what level.) There is little doubt that this procedure is the best means of obtaining the maximum yield of information from this experiment. It is not feasible to introduce a new subject into the regimen, without obtaining preliminary data during a "normal" (control) period, and a delay in the progress of the experiment for this purpose would not be warranted. We shall take advantage of the situation, therefore, to take a "normal" period.

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It seems likely that one new subject (or perhaps two) should be obtained for preliminary observations, as soon as the outcome of the experimental work of the next two months can be established - i.e., when the analyses of specimens obtained from Subject N.R. shall have been completed and the results examined. The results will be given careful consideration and reported to the sponsors with recommendations for the further design of the experiment.

From the budgetary point of view, it does not seem wise, at this time, to recommend gross changes during the next fiscal year. During the last four months of 1967, the expenditures to be made for the compensation of the experimental subjects, for allowances for food, and other purposes, as well as the cost of analytical services, will be diminished. Whether they will be halved, by virtue of the loss of one of two subjects for this entire period will depend upon the outcome of present observations. It seems unlikely that such a decrease in expenditures will continue through 1968 (or through that portion of it which can now be recognized as necessary to complete the present experiment). Just what will be required to achieve the goal set for these experiments is not evident at this time. The principal investigator is not unduly concerned about the details of the budget so long as it is adequate, and is not at all disturbed by the prospect that prudent planning at this point in this work may result in reduced expenditures and an unexpended balance of funds at the end of 1967. His concern is, rather, for the gathering of the best and most useful information in the shortest possible period of time.

In view of the crucial nature of the experimental objective, both for immediate purposes and for the future, it is recommended that the budget for 1968 be maintained at the level of 1967. It is impossible, in dealing with an experimental program of which the outcome is quite unpredictable, (for the

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that it has entered upon an uncharted area of exploration), to describe the details of the next experiment. The fact is that no clue has been obtained in our prior investigations or in any combination of field investigations that have been made, as to the exact level of the concentration of lead in the air which is required to induce a measurable excretory response (urinary) in a normal, healthy man, under conditions intended to approach those that obtain in the general atmosphere of a community. Much speculation has been indulged in, and much statistical manipulation of data from various sources has yielded certain dubious inferences concerning the physiological effect of the differences that exist between the lead content of the atmosphere in different areas - e.g., urban and rural, but no factual information has been obtained under controlled conditions. We should be prepared, therefore, to seek, at the earliest possible time, a definitive answer to this question, in a crucial, terminal experiment. It is our opinion that this point in this investigation is near at hand, and that we should not be handicapped by a shortage of funds at this time. It is suggested that a verbal report of the findings of these experiments might well be made to representatives of the sponsors toward the end of 1967, as a basis for the consideration of a proposed design for the continuation of the experimental work at a definite rate of expenditure during 1968. This should enable the group concerned, at the beginning of 1968, to anticipate the actual rate of expenditure and to make provision for any alteration, hopefully, some reduction in the rate, that may meet with approval.

With these factors in mind, a budget comparable to that submitted in the proposal for 1967, is appended hereto. In this budget, the assumption is made, without official advice, that the continued support of the U. S. Public Health Service, at the same financial level, will be authorized in November, 1967, when it is up for consideration.

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BUDGETRecommended as the Basis for Expenditures to be Made in 1968Expense

For Personnel (including fringe benefits)	70,000	
For Reagents, supplies, food allowances, etc.	8,800	
For Overhead (proportional share of cost of operating the Laboratory)	30,250	
For Contingencies	7,750	
		\$125,800

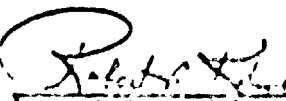
Income

From International Lead Zinc Research Organization	75,000	
From American Petroleum Institute	25,000	
From USPHS Grant AP-000230*	25,800**	
		\$125,800

* Application for renewal of Grant to be considered in November 1967

** Including overhead

Signed:



Robert A. Kahn, M.D., Principal Investigator

July 18, 1967

ILZRO PROJECT SUMMARYIssue Date:
August 1967PROJECT NO. LH-75 TITLE Human Exposure to Particulate Lead Compounds in the Air Under Experimental ConditionsPREVIOUS IDENTIFICATION LH-75 Human Exposure to Ambient Air Concentrations of Particulate LeadCONTRACTOR University of CincinnatiCURRENT CONTRACT January 1, 1967 to December 31, 1967. \$75,000

<u>ILZRO</u>	<u>TEL</u>	<u>OTHER</u>	<u>TOTAL</u>
\$37,500	\$37,500	\$25,000 PHS 25,000 API	\$125,000

CUMULATIVE EXPENSES (to July 31, 1967) \$161,2501968 PROPOSED OR CONTRACT PRICE \$75,0001968 AUTHORIZATION

1967 & Prior Authorizations Uncommitted	none
1968 Proposed Authorization	\$37,500
Undesignated Research Authorization	none
1968 Proposed or Contract Price	\$75,000 (\$37,500 ILZRO; \$37,500 TEL)

MARKET APPLICATIONS Direct to gasoline additive, and indirectly to most other uses of lead.OBJECTIVE To determine the maximum concentration of inorganic lead in the atmosphere that can be inhaled continuously throughout a lifetime by normal, healthy persons without demonstrably progressive accumulations of lead in their body tissue. The results will be used in the defense of the gasoline additive market.RESEARCH REVIEW

1. Current Status Two subjects have completed 20 weeks of exposure to air containing 20 micrograms of lead per cubic meter and a second period of 16 weeks. The third period will be limited to 10 weeks, due to the unavailability to participate longer in the experiment of one of the subjects. The rate of exposure per week has been greatly increased.

2. Projected Research The speeding up of this experiment should result in information that will determine whether a further experiment is required, and at what level.

3. Reports Issued

- Progress Reports - from 1/1/63 to February 1967, six. Last report covered the period 7/31/66 to February 1967.
- Proposal - PROPOSAL TO INTERNATIONAL LEAD ZINC ORGANIZATION FOR THE CONTINUATION, THROUGH THE YEAR 1968, OF THE FINANCIAL SUPPORT OF THE PROGRAM OF RESEARCH IN THE KETTERING LABORATORY, IN THE DEPARTMENT OF ENVIRONMENTAL HEALTH OF THE COLLEGE OF MEDICINE OF THE UNIVERSITY OF CINCINNATI, ON THE PROJECT "HUMAN EXPOSURE TO PARTICULATE LEAD COMPOUNDS IN THE AIR UNDER EXPERIMENTAL CONDITIONS." (dated July 18, 1967).
- Work Statement - none

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ILZNO PROJECT SUMMARY

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DEVELOPMENT REVIEW

1. Pilot Production - not applicable
2. Consumer Evaluation - not applicable
3. Licensing Activities - not applicable
4. Patents - not applicable
5. Publications
 - a. ILZNO - none
 - b. Development associations - none

ECONOMIC INCENTIVE

1. Market Goals - Maintain world market.
2. Applications and Market Volume - Use as gasoline additive.
3. Size of Market Defending - 230,000 tons of lead in U.S. and 51,000 tons in Europe.
4. Competitive Threat - Change refining techniques to eliminate lead additives.