

INTERNATIONAL LEAD ZINC RESEARCH ORGANIZATION

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SCHRADE F. RABTIS
DIRECTOR

September 1, 1965

TO: All Members of the LIA-ILZRO Lead Health and Safety Committee

FROM: Don G. Fowler

SUBJECT: 1966 Budget Meeting of Lead Health and Safety Committee;
October 1, 1965; Sixty East Club; New York City

The Lead Health and Safety Committee will hold its 1966 Budget Meeting at the location specified above on Friday, October 1, as previously announced.

Project Summaries and Extension Proposals to be considered at the meeting are enclosed or will be issued as soon as possible. The new Project Summaries replace the Catalogs of Research issued prior to previous budget meetings. We hope you will find this new format more convenient for project review. Please bring the enclosures to the meeting.

Project or semi-annual reports are being forwarded to you as soon as they are received by ILZRO. Many have already been sent, and we hope to be able to forward the remainder in time for you to review them prior to the meeting.

An Agenda for the meeting is attached. We look forward to seeing you on the 1st.

cc: Lead Technical Steering Committee

Encl: a. Agenda - including listing of enclosures

b. ILZRO Project Summaries (for all currently active projects, active projects being considered for extension and new projects being recommended).

1966 BUDGET MEETING
OF THE
LIA-ILZRO LEAD HEALTH AND SAFETY COMMITTEE

Date: Friday, October 1, 1966

Time: 9:30 a.m.

Place: Sixty East Club, 60 East 42 Street, New York City

AGENDA

- I. Meeting Called To Order
- II. Approval of Minutes of Previous Meeting
- III. Lead Information Program. Report and Budget for 1966.
- IV. United States Public Health Service Symposium on Total Lead Contamination of the Environment
- V. Recent occurrences in the press
- VI. Other business
- VII. 1966 ILZRO BUDGET

<u>Project</u>	<u>Funds Requested</u>	<u>Proposal or Work Statement</u>	<u>Title and Contractor</u>
LH-75	\$35,000	Yes	Human Exposure to Particulate Lead Compounds in the Air Under Experimental Conditions; University of Cincinnati
LH-79	None	No	Toxicity Testing for Organo-Lead Compounds; Industrial Bio-Test Laboratories, Inc. and The Hine Laboratories, Inc.
LH-86	None	No	Lead Glazes for Dinnerware; Rutgers, The State University
LH-94	34,280.26	Yes	Study of the Biological Basis for Lead Intoxication; Harvard Medical School
LH-104	None	No	Toxicity Study of Ingested Paint Film; Hasleton Laboratories, Inc.

ILZRO PROJECT SUMMARYIssue Date:
September 1, 1965PROJECT NO. - LH-75 TITLE - Human Exposure to Particulate Lead Compounds in the Air Under Experimental ConditionsPREVIOUS IDENTIFICATION - LC-75 - Human Exposure to Ambient Air Concentrations of Particulate LeadCONTRACTOR - University of Cincinnati, Cincinnati, OhioCURRENT CONTRACT - 1/1/65-12/31/65, \$35,000, 1965 BudgetCUMULATIVE EXPENSES (to June 30, 1965) \$86,0001966 PROPOSED OR CONTRACT PRICE \$35,000 1966 PROPOSED BUDGET \$35,0001966 AUTHORIZATION

1965 & Prior Budgets Uncommitted	None
1966 Proposed Budget	\$35,000
Undesignated Research Fund	None
1966 Proposed or Contract Price	\$35,000

MARKET APPLICATIONS - Direct to gasoline additive, and indirectly to most other uses of lead.OBJECTIVE - Defend gasoline additive market.RESEARCH REVIEW

1. Current Status - Estimated one half to two thirds work accomplished.
2. Projected Research - Continue as needed to insure this market.
3. Reports Issued
 - (a) Progress Reports
 - 1 - Number of progress reports issued from 1/1/63 to 8/19/65, three
 - 2 - Last report No. 3 - dates of period covered 6/1/64 to 6/1/65

(b) Proposal - (LH-75) PROPOSAL TO INTERNATIONAL LEAD ZINC ORGANIZATION FOR THE CONTINUATION, THROUGH THE YEAR 1966, OF THE FINANCIAL SUPPORT OF THE PROGRAM OF RESEARCH OF 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" (* Officially changed, as of July 1, 1965, to that above.)

(c) Work Statement - NoneDEVELOPMENT REVIEW

1. Pilot Production - Not applicable
2. Consumer Evaluation - Not applicable
3. Licensing Activities - Not applicable
4. Patents - Not applicable
5. Publications - Not applicable
 - (a) ILZRO - None
 - (b) Development Association - None

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ILZRO PROJECT SUMMARY - LHT5ECONOMIC INCENTIVE

1. Market Goals - Maintain world market.
2. Applications and Market Volume - Use as gasoline additives.
3. Size of Market Defending - 200,000 tons of lead in U.S.A. and 51,000 tons in Europe.
4. Competitive Threat - Change refining techniques to eliminate lead additives.

ILZRO PROJECT SUMMARY

Issue Date:
September 1, 1965

PROJECT NO. - LH-79 TITLE - Toxicity Testing for Organo-Lead Compounds
PREVIOUS IDENTIFICATION - LC-79 - Toxicity Testing for Organo-Lead Compounds
CONTRACTOR - Industrial Bio-Test Laboratories, Inc.
 The Hine Laboratories Inc.

CURRENT CONTRACT - No contract needed.

CUMULATIVE EXPENSES (to June 30, 1965) \$1,650

1966 PROPOSED OR CONTRACT PRICE - None 1966 PROPOSED BUDGET - None

1966 AUTHORIZATION

1965 & Prior Budgets Uncommitted	\$ 8,350
1966 Proposed Budget	25,000
Undesignated Research Fund	none
1966 Proposed or Contract Price	\$25,000

MARKET APPLICATIONS - Lubricants, biocides, fungicides, and others mentioned for LC-18 and LC-28.

OBJECTIVE - To provide toxic classification that will satisfy legal requirements for new materials.

RESEARCH REVIEW

1. Current Status - Six compounds have been completed.
2. Projected Research - To test as compounds become available through TNO and Natick.
3. Reports Issued
 - (a) Progress Reports - None
 - (b) Proposal - None
 - (c) Work Statement - None

DEVELOPMENT REVIEW

1. Pilot Production - Not applicable
2. Consumer Evaluation - Not applicable
3. Licensing Activities - Not applicable
4. Patents - Not applicable
5. Publications - Not applicable
 - (a) ILZRO - None
 - (b) Development Association - None

ECONOMIC INCENTIVE

1. Market Goals - See LC-18 and LC-28.
2. Applications and Market Volume - See LC-18 and LC-28.
3. Size of Market Defending - See LC-18 and LC-28.
4. Competitive Threat - See LC-18 and LC-28.

ILZRO PROJECT SUMMARY

Issue Date:
September 1, 1965

PROJECT NO. - LH-86 TITLE - Lead Glasses for Dinnerware

PREVIOUS IDENTIFICATION - ULC-13 - Lead Glasses for Dinnerware

CONTRACTOR - Rutgers, The State University

CURRENT CONTRACT - 9/1/65-8/31/66, \$7,178, 1965 Budget

CUMULATIVE EXPENSES (to June 30, 1965) - : \$3,500

1966 PROPOSED OR CONTRACT PRICE - None

1966 PROPOSED BUDGET - None

1966 AUTHORIZATION

1965 & Prior Budgets Uncommitted	None
1966 Proposed Budget	None
Undesignated Research Fund	\$1,655
1966 Proposed or Contract Price	None

MARKET APPLICATIONS - All civilized countries use glazed dinnerware.

OBJECTIVE - To defend present market and expand lead use by assurances of safety with proper usage.

RESEARCH REVIEW

1. Current Status - Half of the proposed work is completed as of now.
2. Projected Research - Concluding year of two year project.
3. Reports Issued
 - (a) Progress Reports
 - 1 - Number of progress reports issued from 9/1/64 to 6/1/65, two
 - 2 - Last report No. 2 - dates of period covered 3/1/65 to 6/1/65
 - (b) Proposal - not applicable
 - (c) Work Statement - None

DEVELOPMENT REVIEW

1. Pilot Production - Not applicable
2. Consumer Evaluation - Not applicable
3. Licensing Activities - Not applicable
4. Patents - Not applicable
5. Publications
 - (a) ILZRO - None
 - (b) Development Associations - None

ECONOMIC INCENTIVE

1. Market Goals - All glazed china dinnerware throughout the world.
2. Applications and Market Volume - No data on worldwide usage.
3. Size of Market Pending - 16,000 to 20,000 tons as lead in U.S.A.
4. Competitive Threat - Non-lead containing glasses. Threat of government restriction in several countries.

ILZRO PROJECT SUMMARYIssue Date:
September 1, 1965PROJECT NO. - LH-94 TITLE - Study of the Biological Basis for Lead IntoxicationPREVIOUS IDENTIFICATION - ULC-16 - Study of the Biological Basis for Lead IntoxicationCONTRACTOR - Harvard Medical SchoolCURRENT CONTRACT - 1/1/65-12/31/65, \$34,280.26, 1965 BudgetCUMULATIVE EXPENSES (to June 30, 1965) - \$8,570.261966 PROPOSED OR CONTRACT PRICE \$34,280.26 1966 PROPOSED BUDGET \$34,280.261966 AUTHORIZATION

1965 & Prior Budgets Uncommitted	none
1966 Proposed Budget	\$34,280.26
Undesignated Research Fund	none
1966 Proposed or Contract Price	\$34,280.26

MARKET APPLICATIONS - To all lead markets and uses.OBJECTIVE - To provide fundamental understanding of the toxic mode of action of lead in biological systems.RESEARCH REVIEW1. Current Status - A start has been made in the development of tools and techniques of investigation. Application is being made to blood, protein and enzyme systems.2. Projected Research - Continue as above.3. Reports Issued(a) Progress Reports

- 1 - Number of progress reports issued from 1/1/65 to 8/1/65, one.
- 2 - Last report No. 1 - dates of period covered 4/1/65 to 8/1/65

(b) Proposal - LH-94 Proposal For The Study of The Biological Basis For Lead Intoxication(c) Work Statement - NoneDEVELOPMENT REVIEW

1. Pilot Production - Not applicable
2. Consumer Evaluation - Not applicable
3. Licensing Activities - Not applicable
4. Patents - Not applicable
5. Publications - Not applicable
- (a) ILZRO - None
- (b) Development Associations - None

ECONOMIC INCENTIVE1. Market Goals - Defense of markets such as TEL, paint, can solder, presently assailed by allegations of toxic reaction. Expand lead use into areas, such as auto body painting, where allegations of toxic hazards mitigate against use.

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ILZPO PROJECT SUMMARY - LX-94

2. Applications and Market Volume - All lead uses.
3. Size of Market Defending - Application to all lead markets.
4. Competitive Threat - Defensive against competition and legal restrictions.

ILZRO PROJECT SUMMARYIssue Date:
September 1, 1965PROJECT NO. - LH-104 TITLE - Toxicity Study of Ingested Paint FilmPREVIOUS IDENTIFICATION - ULH-15 - Toxicity Study of Ingested Paint FilmCONTRACTOR - Hasleton Laboratories, IncorporatedCURRENT CONTRACT - NoneCUMULATIVE EXPENSES (to June 30, 1965) - None1966 PROPOSED OR CONTRACT PRICE \$9,9001966 PROPOSED BUDGET - None1966 AUTHORIZATION

1965 & Prior Budgets Uncommitted	\$9,900
1966 Proposed Budget	None
Undesignated Research Fund	None
1966 Proposed or Contract Price	\$9,900

MARKET APPLICATIONS - Paint pigments.OBJECTIVE - To raise from 1% total lead the present restriction on paint for interior use. To help create a better climate of opinion for lead paints in general.RESEARCH REVIEW

1. Current Status - Contract not signed.
2. Projected Research - Joint sponsorship with National Paint, Varnish and Lacquer Association and advice from several government agencies.
3. Reports Issued
 - (a) Progress Reports - None
 - (b) Proposal - None to be considered.
 - (c) Work Statement - Not applicable

DEVELOPMENT REVIEW

1. Pilot Production - Not applicable
2. Consumer Evaluation - Not applicable
3. Licensing Activities - Not applicable
4. Patents - Not applicable
5. Publications - Not applicable
 - (a) ILZRO - None
 - (b) Development Associations - None

ECONOMIC INCENTIVE

1. Market Goals - Primary: Interior paints, with estimated potential of 10,000 tons new lead use. Secondary: Miscellaneous uses, such as auto body finishes.
2. Applications and Market Volume - Paint use is increasing with present sales in excess of two billion dollars per year.

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ILZRO PROJECT SUMMARY - LH-104

3. Size of Market Defending - Present U.S. about 50,000 tons per year.
4. Competitive Threat - All non-lead pigments. Existing and proposed legal restrictions.

PROGRESS REPORT - PROJECT NO. LH-75

INVESTIGATION OF HUMAN EXPOSURE TO PARTICULATE LEAD COMPOUNDS
IN THE AIR UNDER EXPERIMENTAL CONDITIONS

The work outlined in previous reports of progress, the last of which was dated September 10, 1964, has been directed primarily toward the determination of the maximum concentration of ideally respirable (that is, particles of lead too small to be deposited in the upper respiratory tract) inorganic lead in the atmosphere, that can be inhaled continuously throughout a lifetime by normal, healthy persons, without demonstrably progressive accumulation of lead in their bodily tissues.

The approach to this problem is patterned on the results of balance experiments (intake of lead in food and beverages, and output in the feces and urine) carried out previously with human subjects under various conditions. In the present experiment, such subjects, after preliminary observation of their lead metabolism under normal conditions, are subjected to the inhalation of air containing lead in a known concentration over periods of time sufficient to demonstrate the occurrence or non-occurrence of a physiological response in the form of an increase in the urinary output of lead. (This response can be detected before any other in the intact human organism.) It is postulated, on good grounds, that the response of human beings to continuous exposure of this type can be determined with approximate accuracy by extrapolation from the results of regular incremental increases in the duration of intermittent exposure - that is, x hours of exposure per day for a suitable time, followed by $2x$, $3x$ and $4x$ hours of exposure, for comparable periods of time, will yield a series of points on a curve which can be

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extended to 24 hours per day, every day.

In a continuation of previous experiments, Subjects N. K. and S. S., in essentially parallel experiments, have been subjected to exposure to lead sesquioxide dispersed in the air of the two respiratory chambers in particles ranging from 0.01 to 0.18 micron in diameter (mean size 0.05 micron) in the concentration of approximately 10 micrograms of lead per cubic meter. (After preliminary control observations, over a period of months prior to the year 1965), these subjects were introduced into the chambers for 3 hours on every other day (10.5 hours per week) over the period of 12 weeks. Subsequently the duration of the exposure per day was doubled, trebled, and further multiplied until, at present, August 18, 1965, one of the subjects (N. K.) is spending 63.0 hours per week, in the chamber, while the other (S. S., who started a bit later) is spending 52.5 hours per week, both having passed through periods of approximately 16 weeks of exposure for 10.5, 21, 31.5 and 42 hours per week, respectively, while Subject N. K. was subject to, additionally 52.5 hours per week for 16 weeks, before undergoing the present phase of the experiment.

There has been no demonstrable excretory response on the part of either subject to the experimental regimen. That is to say that the quantity of lead absorbed daily in the lungs of these subjects has not been sufficient under these conditions to be demonstrated in the face of the variability of the urinary excretion of lead from day to day induced by the absorption from the alimentary tract. Or to be still more specific, the quantities of lead absorbed from the alimentary tract from day to day are so much larger (they can be expected to be much more variable, also) than the quantities absorbed daily from the lung that the latter cannot be detected.

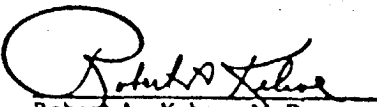
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It is necessary to obtain a response, and in fact to obtain a series of increasing excretory responses, in order to obtain the data for extrapolation from intermittent to continuous exposure. Therefore the experiment must be continued in increasing increments of severity (concentration of lead in air and duration of exposure) until such data have been obtained.

One would wish to expedite the experimental procedure so as to obtain definitive results more promptly and at lesser cost. However, in view of the total lack of experimental precedent, and because of the risk of overshooting the mark (in terms of concentration of lead in air) and thus rendering the subjects unfit for further observations, it seems wise, at this time, to follow the original experimental design during the coming year. If this is done, and if it is necessary, as seems likely, to go beyond the level of 10 micrograms of lead per cubic meter of air in order to obtain an excretory response, the procedure will be that of beginning the new level of exposure at a point, in terms of concentration and time, which is judged to be equivalent to the next serial increment of increase in intensity. Once a response has then been obtained and stabilized (other data indicate that a plateau of response will have been reached in 16 weeks, at most), the course is set for the addition of further points in a curve which will yield the approximate value for continuous exposure. There does not appear, at this time, to be a short cut to this result, and in view of the investment of time and money in this experiment and in the metabolic evidence on which the experiment is founded, it would seem unwise, now, to alter the design. However, at the end of this year (1965), the experimental data will be reviewed critically, as a means of checking the experimental design and of affecting such reduction of time, effort and monetary expenditure as may be feasible. Such modification of procedure as may seem feasible and wise will be communicated to the sponsors for comment and criticism.

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so as to achieve the maximum benefit from the collective critique. Considering the present situation of the principal investigator (on leave in the service of Pan-American Health Organization for the next three months) as well as the present stage of the experiment, it is believed that no useful purpose would be served at this time by assembling the data that would merely illustrate the negative results of the experiment as conducted up to this point. It should be emphasized, perhaps, that the very negativity of the results, in relation to the point of significance that remains to be established is an extremely important finding.


Robert A. Kehoe, M.D.
Principal Investigator

Date: August 18, 1965

LH-75

LH-75

PROPOSAL TO INTERNATIONAL LEAD ZINC ORGANIZATION
FOR THE CONTINUATION, THROUGH THE YEAR 1966, OF THE
FINANCIAL SUPPORT OF THE PROGRAM OF RESEARCH OF
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"

On October 3, 1962, the general experimental procedure of this project, together with the details of a specific experiment to be carried out in 1963, were described in detail. Further proposals, relating to the continuation of the work, were made on September 4, 1963 and on September 10, 1964. The work has gone on in essential accordance with the purposes and procedure described in these proposals, and is to be continued in the year 1966 along similar lines indicated herein.

The immediate goal of the experimental work in 1965 was that of defining, through human experience, the maximum concentration of ideally respirable and absorbable (i.e., pulmonary absorption, exclusively) particulate lead in the ambient atmosphere to which normal, healthy, human subjects might be subjected, continuously and for indefinitely prolonged periods of time, without incurring the potential risk of a demonstrable degree of accumulation of lead in their bodily tissues.

The experimental principle involved the exposure of two human subjects, in parallel respiratory chambers, to air containing lead (approximately 10 micro-
* Officially changed, as of July 1, 1965, to that above.

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grams of Pb, as lead sesquioxide, per cubic meter) dispersed in minute particles (ranging in diameter from less than 0.01 to 0.18 microns, with the mean diameter of 0.05 microns), on an intermittent schedule of increasing duration (3 hours per day every other day for approximately 16 weeks, i. e., 10.5 hours per week; 6 hours per day every other day for approximately 16 weeks, i. e., 21.0 hours per week; and so on to 31.5, 42.0 hours, etc.) until the effect of the exposure became evident through a slight (statistically demonstrable) increase in the output or concentration of lead in the urine, presumably (as judged by earlier experiments) without demonstrable increase in the concentration of lead in the blood, of the subjects.

During 1965, these observations have continued as scheduled, except for necessary adaptation of the periods of exposure to the tolerance of the subjects for disruptions of their daily lives. That is, when the schedule reached the point of requiring the subjects to spend more than 12 hours per day in the chamber (on alternate days) it became necessary to shift to daily periods of exposure. Obviously, also, the continuation of the family life of the subjects required, at least, one day per week of freedom from exposure. The result was a new schedule, involving the proper number of hours of exposure per week subdivided into equivalent periods on six of the seven days of each week. At this time (August 1965), one of the subjects (N. K.) is spending 63 hours per week in the chamber, while the other (S. S.) (who was taken on late as an experimental subject, as reported previously) is spending 52.50 hours per week.

Inasmuch as neither of these subjects has yielded the slightest response to the graduated levels of experimental exposure, the experiment is to continue as long as possible at the present level of lead concentration in air. It is not anticipated at

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present that it can go far beyond 12 hours per day on 6 days per week, with due regard for the comfort and convenience of the subjects. If then no response shall have been obtained, the concentration of lead in the chamber will be increased by a small increment, and the incremental increases in the duration of exposure will be rescheduled, beginning at a level of intensity (time x concentration) that will not duplicate that of previous steps. It will be necessary, obviously, to obtain a response, and such response must be graduated from the least demonstrable intensity through at least three levels in excess of the minimum, in order to provide data for extrapolation to the effects of continuous exposure (24 hours per day on 7 days per week). Accordingly, the experiment may be expected to continue through the entire year 1966.

It is conceivable that the experimental regimen can be modified so as to shorten the time required to obtain definitive results. The means of so doing are under consideration at present, and the entire situation will be explored critically at the end of this calendar year. There is some risk, however, in any radical alteration of the original design of the experiment, in that too sharp an increase in the exposure may yield an excessive response, and threaten, thereby, the further usefulness of the subjects. It was for this reason that the initial level of the concentration of lead in the chamber was set at 10 micrograms per cubic meter - a level which could be counted on (from indirect but satisfactory evidence) to yield negative results at first, with the possibility that there might be a positive response as the time factor progressed toward continuity.

With the present facts and anticipations in mind, the cost of the experimental program in 1966 is expected to be similar to that of 1965. Some economy may be affected, since it seems unnecessary, in future experiments, to analyse

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duplicate samples of the food of the subjects. (The correlation between the lead in the food, day by day, with that in the feces, day by day, is so satisfactory as to enable the former items of data to be eliminated, apparently without introducing an error that is greater than the sampling error. Further statistical work will be necessary to substantiate the facts in this regard with certainty, and this feature of the design will be examined critically at the end of the current year (1965).

Only one other issue arises at this time in the budgetary considerations. The proposal to the Public Health Service, involving their further participation in the support of this project, has been approved in principle, but is dependent upon the availability of funds through Congressional appropriation. It is expected that the funds will be made available, but should this not be the case, it will be necessary either to submit a supplementary proposal to the other sponsors of the program, or to curtail the work.

The following budget is recommended for 1966, on the basis of the expenditures made in 1964, and of those made to date in 1965:

For personnel and services (direct and indirect costs)	\$ 75,000.00
For special reagents, supplies, allowances for food, etc.	5,000.00
Overhead (proportional share of cost of operating the Laboratory)	<u>30,000.00</u>
Total	\$110,000.00

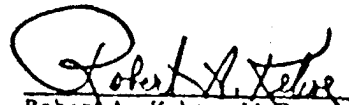
On the assumption that funds will be available from previous sources for the support of this work, the costs would be allocated in round numbers, as follows:

Ethyl Corporation	\$ 25,000.00
E. I. du Pont de Nemours and Company	25,000.00
International Lead Zinc Research Organisation	35,000.00
U. S. Public Health Service	<u>24,000.00</u>
Total	\$109,000.00

While the roughly estimated budget and the equally roughly estimated

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expenditures are not identical, there is little reason to doubt that the expenditures can be held within the estimate.


Robert A. Kehoe, M. Q.
Kettering Laboratory

Principal Investigator

Date: August 18, 1965