

OF THE
LEAD ENVIRONMENTAL HEALTH COMMITTEE
OF THE
INTERNATIONAL LEAD ZINC RESEARCH ORGANIZATION, INC.
SEPTEMBER 14, 1970

In accordance with the notice of June 22, 1970, the 1971 Budget Meeting of the Lead Environmental Health Committee was convened at 9:30 AM, Monday, September 14, 1970 at the Engineers' Club, 32 West 40th Street, New York, New York.

R. C. Bell presided and J. F. Cole served as secretary.

Those in attendance were:

R. C. Bell (Chairman)	Cominco, Ltd.
K. Nelson	American Smelting and Refining Company
L. Cogen	Ametalco, Inc. (Representing Tsumeb Corporation, Ltd.)
E. Gay	Associated Ocel Company, Ltd.
R. Semmens	The Broken Hill Associated Smelters Pty., Ltd.
R. Butler	E. I. duPont de Nemours & Company
D. Diggs	E. I. duPont de Nemours & Company
R. Sugimoto	Houston Chemical Company
H. Sakurai	Mitsubishi Metal Mining Company, Ltd.
H. Tachimori	Mitsui Mining and Smelting Company, Ltd.
J. Calandra	Nalco Chemical Company
J. Darcey	Societe Miniere et Metallurgique de Penarroya
D. Bielstein	St. Joe Minerals Corporation
R. Kubalak	St. Joe Minerals Corporation
J. Sevick	St. Joe Minerals Corporation
F. Warner	U. S. Smelting, Mining and Refining Company

ASSOCIATE MEMBERS

W. Pallies	ESB, Inc.
R. Rogers	Hill and Knowlton, Inc.
S. Hiscock	Lead Development Association
D. Borcina	Lead Industries Association
J. Kimberley	Lead Industries Association
W. Zeek	C. Tennant Sons & Company

ILZRO Staff

D. Carr
J. Cole
S. Radtke

I. Voting Members

The chairman counted fifteen (15) voting members. Note- because several members could not attend the entire meeting, the total number of votes registered was not always 15.

II. Approval of Minutes of Previous Meeting

The minutes of the Spring Meeting of the Lead Environmental Health Committee held in St. Louis, Missouri on April 7, 1970 were unanimously approved as submitted to the Lead Environmental Health Committee.

III. Election of Chairman for 1970-71

Mr. Bell opened the floor for nomination for chairman of the ILZRO Lead Environmental Health Committee for 1970-71. Mr. Nelson nominated Mr. R. C. Bell of Cominco. There being no more nominations, the floor was closed and Mr. Bell was elected unanimously as chairman for 1970-71.

IV. Budget Action on 1970 Lead Environmental Health Research Projects

1. LH-157 Health Study of Lead Workers, Tabershaw-Cooper Associates, \$84,900, (ILZRO, \$42,450, TEL, \$42,450).

Dr. Cole presented the report on the feasibility study and proposal from Tabershaw-Cooper Associates which was presented to the Steering Committee assigned to this project on September 2, 1970. The Steering Committee's recommendation was that ILZRO accept the proposal and that work on the full study begin immediately. Dr. Calandra noted that the feasibility study had taken much longer than was originally anticipated and suggested that there be a performance requirement in such contracts. Dr. Cole agreed that the feasibility study had been delayed and for this reason a full time project would be assigned to this project by the contractor. Dr. Radtke noted that a performance clause is included in all ILZRO contracts.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
15	0	0	\$42,450	\$42,450

V. Budget Action on 1971 Lead Environmental Health Research Projects

1. LH-157 Health Study of Lead Workers, Tabershaw-Cooper Associates, \$84,925, (ILZRO, \$42,462.50, TEL, \$42,462.50).

Since this project will begin immediately it was required that funds be allocated for the second year of this project which will begin in 1971. Dr. Cole pointed out that a proposal for the second year of the study would be submitted to the Environmental Health Committee for their approval before the contract is extended.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
13	0	0	\$42,462.50	\$42,462.50

2. LH-176 ILZRO/TEL Defense, Atomics International Company, \$75,000 (ILZRO, \$37,500, TEL, \$37,500).

Dr. Carr presented a report on his visit to Atomics International Company along with a description of their device for the removal of lead from automotive exhaust using a eutectic salt scrubber. Dr. Carr stated that Atomics International had reached the point in the development of this device at which funds were needed from other industries to convince their own management that such a device may have a future market. Dr. Diggs, Mr. Hall and Mr. Gay were pessimistic about the future of the device but Mr. Kimberley noted that the TEL market was so important as to warrant an attempt to bring any possible solution to fruition. Dr. Diggs stated that he felt that such an expenditure could not be made at this time by DuPont, but that if the device looked more promising in the

future, it may warrant consideration. Mr. Sugimoto commented that he received a report from the National Air Pollution Control Administration regarding their support of the initial development phase on this project. Mr. Sugimoto offered to make this report available to the entire committee. Mr. Kimberley recommended that a sum in the amount of \$37,500 be allocated by ILZRO and that he would attempt to obtain a matching sum from the Lead Industries Association.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
9	0	6	\$37,500	None

3. LH-79 Toxicity Testing of Organolead Compounds, Various Contractors, \$10,000, (ILZRO, \$10,000)

These funds are used on an as-needed basis for toxicity testing of promising new organolead compounds synthesized under the LC-18 program.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
14	0	1	\$10,000	None

4. LH-86 Lead Glazes for Dinnerware, Rutgers University, \$25,000, (ILZRO, \$2,500)

Dr. Cole explained that this project was reinitiated during 1970 because of several recent cases of lead intoxication involving poorly glazed dinnerware and subsequent activity by the U.S. Food and Drug Administration. The current program is designed to compare the ASTM test for the release of lead from glazes with actual use conditions. It was recommended that this project be continued through 1971 in cooperation with the U.S. Potters Association.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
15	0	0	\$2,500	None

5. LH-94 Study of the Biological Basis for Lead Intoxication, Harvard Medical School, \$52,254.00, (ILZRO, \$26,127, TEL, \$26,127)

Dr. Cole noted that Dr. Vallee had become very interested in the current problems besetting the lead industries regarding d-amino-levulinic acid dehydrase. It was also noted that Dr. Vallee had made excellent presentations at the LH-161 Lead Symposium held in Puerto Rico in 1970 and at the April meeting of the Lead Environmental Health Committee. Future plans call for ILZRO to attempt to obtain more public exposure for Dr. Vallee and his work. Dr. Diggs noted that Dr. Vallee's report this year was excellent and urged ILZRO to attempt to have the "prologue" of the report published and also to approach Dr. Vallee with an aim toward having him testify before regulatory groups.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
14	0	1	\$26,127	\$26,127

6. LH-106 Lettering Abstracts of Lead Toxicology, University of Cincinnati, \$8,083.05, (ILZRO, \$8,083.05)

Although the amount requested for this project has been considerably increased for 1971, Dr. Cole recommended that this service be continued. It was pointed out that the \$7500 paid in the past for the total contract by ILZRO, LIA and LDA was not nearly enough to cover the costs of the University of Cincinnati.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
14	0	0	\$8,023.05	None

7. LH-114 Effects of Chronic Plumbism on Neurological Behavior in the Rhesus Monkey, Industrial Bio-test Laboratories, \$55,052.06, (ILZRO, \$27,526.03, TEL, \$27,526.03)

Dr. Cole pointed out that the ILZRO Environmental Health Committee had recommended that neurological testing be continued on the animals which had been fed lead on this project for approximately two years. It was felt that with such a unique group of animals we should attempt to obtain as much neurological information as possible. It was noted, however, that the contractor had recommended that a new set of animals be brought into the study because baseline data electroencephalographic data are not available on the animals which have been undergoing lead exposure. Dr. Calandra offered to see that the full amount of work as outlined in the proposal is carried out if ILZRO would fund this project at approximately the same level as it had been funded in the past. Dr. Calandra also noted that ILZRO has been paying only half the actual cost of this research in the past.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
12	0	2	\$12,939	\$12,939

8. LH-138 Study of Lead Release From PVC Piping, National Lead Company, \$10,000, (ILZRO, \$10,000)

The purpose of this study is to obtain National Sanitation Foundation approval for a lead stabilized PVC pipe in potable water. Research is now underway at the National Lead Company's Hightstown, New Jersey laboratories in an attempt to produce a low lead release lead stabilized PVC pipe. Should this work produce a suitable pipe, ILZRO would support the testing required by the National Sanitation Foundation.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
13	0	0	\$10,000	None

9. LH-152A Blood Lead Analysis Study, Societe de Metallurgique de Pen-arroyc, No Funds Requested.

Mr. Darcey stated that a request for funds could not be made at this time pending the outcome of preliminary test with the graphite oven. It was noted that a future request for funds may come to ILZRO which could be financed from the Undesignated Research Authorization.

10. LH-152B Blood Lead Analysis Study, Environmental Sciences Associates, Inc., \$24,025, (ILZRO, \$12,012.50, TEL, \$12,012.50)

Mr. Nelson pointed out that anodic stripping voltammetry (ASV) is an exciting new development for the analysis of lead. However, he questioned the need for a portable analytical instrument and stated that the costs are not likely to be less than with already existing methods. He suggested that ILZRO not support this work in view of our ongoing work with LH-152B and Federal involvement in an automated ASV system.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
0	12	1	None	None

11. LH-153 Information on Lead Environmental Health Activities in Europe, Fowler Davies & Company, \$7,000 (ILZRO, \$3500, TEL, \$3500)

Dr. Cole recommended that this project be extended through 1971. Dr. Diggs commented that he would like to see more emphasis placed on political occurrences in Europe with regard to environmental health activities. Dr. Cole noted that he would inform Mr. Fowler of this request.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
13	0	0	\$3500	\$3500

12. LH-159 Study of the Effect of Lead on the Respiratory Activity of Erythropoietic Cells, Ohio State University, \$15,809 (ILZRO, \$7,904.50, TEL, \$7,904.50)

Dr. Cole noted that this contractor had performed his obligations very well in that the reports were quite good and on time. However, he expressed doubt that the research would achieve the desired objectives. Dr. Roush concurred in this noting that the contractor had spent a great deal of time in perfecting methods which the committee had understood were already perfected.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
0	13	0	None	None

13. LH-160 Effects of Particle Size on the Absorption of Lead in Humans, University of Cincinnati, \$32,366 (ILZRO, \$31,183, TEL, \$31,183)

Dr. Cole commented that the lead industries owe Dr. Kehoe, the primary investigator on this project, a great debt for his fine work over the years. However, with the large expenditure involved in this project and the limited amount of useful data which can logically be expected from it, he did not feel that the expenditure would be justified. Mr. Nelson supported this view. Dr. Roush noted that this experiment would provide useful information, but that like other ILZRO Environmental Health projects this information may not have immediate value.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
0	6	7	None	None

14. LH-162 Human Variations in susceptibility to Lead, Clinica Del Lavoro, University of Milan, \$36,785 (ILZRO, \$18,392.50, TEL, \$18,392.50)

Dr. Cole referred to a letter received just prior to the meeting from Dr. Vigliani, explaining that work is now underway on this project. Dr. Cole explained that a construction strike in Italy had slowed work on a new section of the laboratory causing nearly six months delay on the project. Dr. Vigliani requested that a greater sum be allocated for 1971 than for 1970 because of the increased expenses caused by inflation and also for the purchase of an anodic stripping voltammetry instrument. The suggestion was made that ILZRO retain ownership to all such equipment purchased with ILZRO funds. Dr. Radtke agreed that this should be made a part of all ILZRO contracts. The proposal for 1971 will include an investigation of individuals susceptibilities to the effect of lead on d-aminolevulinic acid and d-aminolevulinic acid dehydrase.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
7	4	2	\$18,392.50	\$18,392.50

15. ULH-26 Study of the Effect of Lead on the Kidney, University of Goteborg, \$32,000 (ILZRO, \$16,000, TEL, \$16,000)

Dr. Cole noted that the question of the effect of chronic exposure to lead on the kidney was a subject of major concern at the LH-161 lead symposium in Puerto Rico. The question of whether chronic exposure can cause lead nephropathy is one which continues to plague the lead industry and about which little is actually known. Questions were raised regarding the exposure of the subjects since it was not clear in the proposal that subjects with low, intermediate and high exposures to lead are to be included in the investigation. It was recommended that subjects with all types of exposure be included so that an "effective dosage" could be determined. Further, there was an expression that the amount of money requested was too great for the amount of work to be accomplished. Also it was recommended that ILZRO retain ownership to any equipment purchased with ILZRO funds. There were three votes taken on this project. The first vote was on the proposal as written.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
2	2	9	None	None

The second vote was on the proposal as written with the understanding that ILZRO would retain ownership to any equipment purchased.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
4	5	0	None	None

The third vote was on the notion that the proposal be accepted on the condition that subjects with a graduation of exposures are included in the project and that the entire project can be accomplished for \$20,000 in 1971.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
8	1	4	\$10,000	\$10,000

15. ULM-27 Economic Comparison of Methods for Analysis of Lead in Blood, Environmental Health Laboratories, \$26,000 (ILZRO, \$26,000)

Dr. Cole recommended that this proposal be rejected because of the overall demand upon our available funds. He pointed out, however, that the study was an interesting one and might provide useful information, but that its priority must be considered low.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
0	13	0	None	None

16. ULM-28 An Evaluation of Aromatic and Metallic Substances in Selected Urban Atmospheres, University of Cincinnati, \$93,814, (ILZRO, \$46,920.50, TEL, \$46,920.50)

Dr. Cole recommended that ILZRO support 1/3 of the total cost of this project with an attempt to obtain support for the remainder from the American Petroleum Institute and the U.S. Public Health Service. Dr. Diggs noted that he could not support an expenditure for the entire amount, but because of the political benefit which might be gained from such a project, he recommended that ILZRO support 1/3 of the total cost of the program.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
10	1	2	\$15,640.17	\$15,640.17

17. ULM-29 Effects of Lead and Insecticides on Avian Reproduction, California Fish & Game Department, \$12,214.34 (ILZRO, \$6,107.17, TEL, \$6,107.17)

Dr. Cole recommended that the project be rejected since the preliminary work submitted by the proposed contractor seemed to answer the questions posed in the research proposal. Also it was noted that joint financing was not assured and that there had been difficulty in obtaining cooperation from the California Fish & Game Department, in an effort for joint financing. Dr. Diggs noted that he favored assisting state conservation departments with their problems when they involve lead.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
1	12	0	None	None

18. ULM-30 Epidemiological Study of Effect of Airborne Lead on Heme Synthesis, No Contractors yet, \$50,000 (ILZRO, \$25,000, TEL, \$25,000)

Dr. Cole explained that this project came about because of a suggestion of Dr. John Goldsmith that such data is needed so that the effect of ambient exposure to lead on delta aminolevulinic acid excretion can be ascertained. The Venture Analysis is presented to the committee as paraphrased from a report by a subcommittee appointed by the Lead Liaison Committee to design a protocol for this work. Dr. Cole explained that this project would not be supported unless it was recommended by the Full Lead Liaison Committee.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
2	2	1	\$25,000	\$25,000

that such a phenomenon has been recognized for years in the lead industry and that it results from very high body burdens of lead in poisoned workers. Chelation therapy removes only a small portion of the total body burden of lead. After therapy is discontinued the body again strives for equilibrium with respect to lead and blood lead concentrations go up and symptoms reoccur. It was the opinion of the committee that the research work with baboons would provide little new information regarding lead intoxication.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
0	11	0	None	None

23. ULH-33 Concentration of Lead in the Atmosphere and Population in Japan, Keio University, \$57,400 (ILZRO, \$28,700, TEL, \$28,700)

Dr. Radtke explained that the project was deemed to be of great importance in Japan because of the recent publicity given to a finding by a group of physicians stating that many persons residing near a heavily traveled intersection were ill with lead poisoning. This group reported some rather high values for lead in blood and urine. After much discussion, concerning the usefulness of the study, Mr. Gay suggested that ILZRO supply funds for carrying out the study but that the Japanese producers provide a fund for the required equipment.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
8	0	2	\$15,700	\$15,700

24. Undesignated Research Authorization, \$50,000 (ILZRO, \$25,000, TEL, \$25,000)

Dr. Cole pointed out that the funds authorized under Undesignated Research Authorization would be used for projects which come up during the year. Each project, however, will be submitted to the full Environmental Health Committee for a letter ballot.

Vote			1971 Funds Recommended	
In Favor	Opposed	Abstentions	ILZRO	TEL
9	0	0	None	None

25. Dr. Roush presented a proposal just received by him from the Ethyl Corporation to determine if lead methylates in a natural aqueous environment as has been recently found with mercury. Because the committee had such little time to review the proposal, Dr. Cole suggested that it be circulated to the entire committee and that a letter of ballot be taken. If the proposal is accepted the funds will be taken from the Undesignated Research Authorization.

- VI. Budget Action on 1971 Zinc Environmental Health Research Projects
 UZH-1 Carcinogenicity of Zinc, University of Cincinnati, \$35,000, (ILZRO, \$35,000)

Dr. Cole explained that this project was being presented to the Lead Environmental Health Committee because ILZRO does not have

a Zinc Environmental Health Committee. This project was recommended because of allegations by Dr. Halme of Finland that low levels of zinc, such as found in drinking water, cause cancer in laboratory animals. Dr. Cole noted that Halme's work had been considered as poor by a number of reviewers but the fact that some evidence exists that zinc may cause cancer should be of concern to the zinc industry. Also since it will take at least 3 years to produce data to either refute or corroborate Halme, work should begin soon.

It was the opinion of several members of the committee that such poor work should not require ILZRO to spend large sums to refute it. Also, epidemiological studies were suggested to answer Halme's claim. Dr. Cole cited LH-157 in noting that such studies are very difficult and very costly.

<u>Vote</u>		Abstentions	<u>1971 Funds Recommended</u>	
In Favor	Opposed		ILZRO	TEL
0	8	2	None	None

VII. Report on Other ILZRO Environmental Health Programs

Because of the late hour and the fact that most other research projects had been discussed during the session this agenda item was cancelled.

VIII. Adjournment

There being no further business to come before the committee, the meeting was adjourned at 6:00 P.M.

Submitted by:

Jerome F. Cole

J. F. Cole, Sc. D.

7-14162

7-14162

UNIVERSITÀ DEGLI STUDI
ISTITUTI CLINICI DI PERFEZIONAMENTO

CLINICA DEL LAVORO "LUIGI DEVOTO"

DIRETTORE PROF. ENRICO C. VIGLIANI

Dr. Jerome F. Cole
Manager, Environmental Health
International Lead Zinc Research
Organisation, Inc.
292, Madison Avenue
New York, N.Y. 10017
U.S.A.

20192 MILANO 28th August, 1970
VIA S. BARNABA, 8
57.60.91 - 58.16.10

Prot. 658/ECV/kw

Dear Doctor Cole,

Enclosed you will find the scientific and financial programmes for the extension to the research project on "Human Variations in Susceptibility to Lead" for the period from 1st July, 1971, to 30th June, 1972.

Of course, in addition to the work planned in the extension, we shall continue the work begun in July 1970 and which might not be completed by June, 1971. We shall try to put into operation the new method of lead analysis with anodic stripping voltmetry, which you suggested and which seems very promising.

I very much hope that our programme will be accepted by ILZRO's Environmental Health Committee.

The new floor which has been added to the laboratories of the Clinica del Lavoro is now almost complete and we are now ready to start work on the programme for 1970.

As you will see, the financial budget will amount to \$30,000 instead of \$25,000, but this is due to the rise in all costs which has occurred in Italy in the last few months. In addition to the financial budget, we should like to purchase the MASA 2014 multiple anodic stripping analyzer. From Environmental Sciences Associates brochure we see that the MASA 2014/electronic and cell holder costs \$3,950, the MASA 2014-4/4 cell extension \$2,700 and the replacement parts for the cell holder \$221.25. Would it be possible to have some assistance from the ILZRO to buy this instrument?

We trust that the delay in sending you the programme for 1971 will not cause any inconvenience. The reason for the delay is that we have been extremely busy in the past months with a complete renovation of the Clinica del Lavoro, and also I wished to thoroughly discuss with Professor Pernis the lines along which our investigation could be carried out in the second year of the research project.

With best personal regards.

Yours sincerely,

EPI 000218

N11662.01

Extension of the Research Project on "Human Variations in Susceptibility to Lead" for the period from 1st July, 1971, to 30th June, 1972.

During this period the proposed research will be performed with the main aim of investigating the possible effect of lead on urban populations not professionally exposed to lead.

Action of normal urban lead on heme synthesis and life span of red cells

A recent report in the literature by Hernberg and Nikkanen (Lancet, i:63, 1970) raises the possibility that lead absorption that may occur under normal urban conditions may be sufficient to inhibit some enzymes involved in heme synthesis like ALA-dehydrogenase. The basis of this assumption rests on an observed inverse correlation of ALA-dehydrogenase levels and blood lead in a group of individuals not occupationally exposed to lead.

We propose to control this condition on large samples of the urban population in Milan which would also include some individuals such as traffic wardens, etc., who might have been exposed more than the others to the absorption of some lead.

The ALA-dehydrogenase activity of erythrocytes will be measured with due attention to the possible criticism of Bonsignore's method, taking into account the modifications of this method that have now been tested in the Institute of Biochemistry of the University of Genoa by Bonsignore and his colleagues. It is foreseen that this methodological work will be completed before July 1971.

With regard to the measurement of blood lead, whose accuracy is equally important to obtain a meaningful correlation with the ALA-dehydrogenase levels, particularly at low concentrations of the metal in blood, different methods will be used, including not only a dithizone assay as performed by Hernberg and Nikkanen, but also recent techniques of atomic absorption and, if possible, the electrolysis method. Here again, the time before 1st July, 1971 will be very useful for putting these methods in optimal working conditions.

If an inverse correlation between blood lead and ALA-dehydrogenase levels is obtained, then the individuals at the lower right end of the curve (i.e., those with relatively higher blood lead levels and relatively lower ALA-dehydrogenase levels) will be sorted out for further investigation.

In these individuals one or more cycles of treatment with EDTA will be performed in order to see whether there are parallel changes of lead blood levels and ALA-dehydrogenase activity. This will be done with the aim of investigating whether in fact the lowest levels of ALA-dehydrogenase in an urban population are connected with a relatively higher lead intake.

Finally, in some volunteer members of this group of individuals, the life span of circulating erythrocytes will be determined with the method of chromium-labelled erythrocytes with the aim of obtaining information on the possibility that in these subjects the apparent inhibition of ALA-dehydrogenase, presumed to be induced by lead, is in fact influencing the erythropoietic system. For this latter purpose we also plan to obtain a complete profile of the different enzymes in erythrocytes of different density (Marks et al., Proc. Natl. Acad. Sci., 50:336, 1963) to get some information on the average age of the erythrocyte population in these individuals.

It goes without saying that all this work will be performed in addition to ordinary hematological studies, like hemocytometry, hematocrite, study of the size and shape of red blood cells, reticulocyte counts, search for basophilic stippled cells, etc.

In connection with this line of research, which will be mainly epidemiological, another line will be pursued intended to investigate the possibility that ALA-dehydrogenase levels of different individuals may have a different sensitivity to the action of lead.

This problem will be approached in the first instance by testing the blood of different normal individuals after addition of lead in vitro. However, we must keep in mind that inhibition of ALA-dehydrogenase by lead in vivo might be a more complex process, as shown by the relative persistence of depressed enzyme levels even a long time after termination of exposure to lead in industrial workers.

Recent unpublished work by Bonsignore et al. has raised the possibility that the action of lead on ALA-dehydrogenase "in vivo" may be partly mediated by the induced synthesis by the metal of a protein inhibitor of the enzyme. This point needs further investigation because if it were substantiated it might be appropriate to try to detect and measure this inhibitor even in persons not industrially exposed to lead, and particularly in that group of normal individuals which we have indicated before as corresponding to those who might have relatively higher levels of lead in the blood and relatively lower levels of ALA-dehydrogenase.

Financial Budget for the Extension of the Research Project on "Human Variations in Susceptibility to Lead" for the period from 1st July, 1971, to 30th June, 1972

Personnel:

- One biochemist, 60% of the time	US \$ 6,000
- One analytical chemist, 60% of the time	" " 6,000
- One physician, 60% of the time	" " 6,000
- One laboratory technician, full time	" " 6,000

Consultant Services:

" " 2,000

Supplies:

" " 2,000

Travel, domestic:

" " 500

Publication costs:

" " 500

Outpatient costs:

" " 1,000

Total

US \$ 30,000

Purchase of MASA multiple anodic stripping analyzer

US \$ 6,875

Grand Total

US \$ 36,875

N11662.03

EPI 000222

VISIT REPORT

By: J. F. Cole

Date: September 1, 1970

Location: The Hine Laboratory
San Francisco, California

Person Visited: Dr. C. H. Hine

Subject: ULH-32 Evaluation of Chronic Toxicity of Triphenyllead Acetate

Although a proposal from Lifestream Laboratories has been submitted to the Lead Environmental Health Committee for support in 1971, I found out quite recently that they have gone out of business. The proposal was the best of three received last year when we proposed that the work be financed by the organolead licensees. A proposal was also received from the Hine Laboratory but was not nearly as comprehensive and much more expensive.

The Hine Laboratory, however, has an excellent reputation in toxicological investigations and it was thought that it might be valuable to discuss the project with Dr. Hine in order to include more work in his proposal and possibly prevail upon him to reduce his price.

After discussions I received a verbal commitment from him to include inhalation toxicity testing and to reduce the cost of the oral feeding study. Dr. Hine suggested that we also add lead in tissue determinations to the overall protocol.

The following is a comparison of the original Hine proposal, the new one and the Lifestream Laboratory proposal:

	<u>Old Hine Proposal</u>	<u>New Hine Proposal</u>	<u>Lifestream Proposal</u>
90 Day Aerosol Inhalation in Rats	Not Included	\$10,000	\$11,000
180 Day Oral Feeding in Rats	\$18,000	\$ 5,000	\$ 5,400
45 Day Dermal Toxicity in Rabbits	\$ 2,000	\$ 2,000	\$ 4,500*
Skin Sensitization in Guinea Pigs	\$ 600	\$ 400	\$ 400
Repeated Insult Patch Test in Humans	Not Included	\$ 1,000	\$ 1,000
Lead Analysis of Tissue	Not Included**	\$ 1,200	Not Included
Totals	\$20,600	\$19,600	\$22,300

* Called for 90 day exposure.

** Not included as a specific item but included in protocol.

Hine had no explanation of why he proposed \$18,000 for the 180 day oral feeding study but said that it might have been mistakenly calculated on the basis of using dogs.

Since Hine has reduced the cost of his proposal so drastically, it is my feeling that we should now give it primary consideration for support in 1971.

JFC

N11662.04

EPI 000223

Proposal To
The International Lead Zinc Research Organization
From
Keio University
Tokyo, Japan

Purpose of Study:

In June 1970, virtually all Japanese newspapers reported that physicians of Hikkawashita Settlement Hospital had claimed an outbreak of lead poisoning among inhabitants in areas of heavy traffic in Tokyo. This report caused panic among Japanese people in relation to a "Public Nuisance". However, a later investigation by a well-established and respected institute, the Occupational Service Center, headed by Dr. Juko Kubota, refuted the results reported by the Settlement Hospital physicians. Nevertheless, the Settlement report which appeared in Japanese newspapers, covering almost a full page, has left a lasting impression on the Japanese populace. Because of this, the Ministry of Commerce declared that TEL must be completely removed from gasoline within five years. In fact, beginning in 1970, the amount of TEL in gasoline was reduced by one-half from the amount used previously, although aromatic hydrocarbons were increased to maintain the octane rating. It would be surprising if the ruling of the Ministry of Commerce will be implemented within such a short period of time.

In this situation, it has become most important to elucidate whether or not the lead in the air of Japanese Cities could cause any significant health hazard to man. With regard to lead in the ambient air of urban communities in Japan, only a very limited number of reports have been published.

This proposed study, therefore, aims to clarify whether or not lead in the ambient air of areas of heavy traffic has any effect on human health in terms of body burden.

General Outline of Methods

In 1965, a report entitled, "Survey of Lead in the Atmosphere of Three Urban Communities", was published in the U.S.A. Subsequently, a study entitled, "Seven Cities Study", was initiated. In general, the proposed study would follow the method used in the "Seven Cities Study". The cities proposed for this study are Tokyo and a limited area of Yokohama. This proposed investigation is much smaller in scope than the Seven Cities Study of the U.S.A.

It is proposed that blood samples be obtained from the Japanese population of different areas of Tokyo, and also from specific occupational groups, such as workers in road construction companies, taxi drivers, policemen and so forth. A total of about 2,000 blood samples for lead analyses would be collected during the study. Urine samples would also be collected and analyzed for coproporphyrin and delta- α -amino levulinic acid. The results obtained would be analyzed statistically with respect to age distribution, sex, residence, and so forth.

Air sampling stations would be selectively located in Tokyo and Yokohama. At the present moment eight stations, routinely operated by the Tokyo Metropolitan Health Department, would be used. In addition, four or five new stations would be established for this study. However, the aforementioned eight stations do not have arrangements for lead sampling: a total of twelve air sampling stations for lead are recommended for the proposed study.

Blood lead analyses would be made by two institutes, the Keio University School of Medicine under Professor Kenzaburo Tsuchiya, and the Occupational Health Center under Dr. Juko Kubota. Air lead analyses would be performed by the

Yokohama National University School of Engineering, directed by Dr. Yoshitaka Kobayashi.

This is a general outline of the work proposed. Subsequently, a detailed plan will be prepared in accordance with the recommendations of the ILZRO Environmental Health Committee.

The program can be initiated by 1 November 1970, or by 1 January 1971 upon advice of the ILZRO Staff.

Cost Analysis

It is envisioned that the study will be completed one year after approval of the proposed program.

1. Personnel Costs

Three full time technicians, 1 year	\$ 6,000.00
Secretary, 1 month	200.00
Three Lab. technicians, 2 month each	1,200.00
Total	<u>\$ 7,400.00</u>

2. Supplies & Equipment

Low temperature ashier (2)	\$16,000.00
High Volume Sampler (12)	10,000.00
Total	<u>\$26,000.00</u>

3. Lead sampling and analyses

Blood (2,000 samples)	\$14,000.00
Air (600 samples)	2,000.00
Coproporphyrin and Δ -ALA in urine (2,000 samples)	8,000.00
Total	<u>\$24,000.00</u>

<u>Grand Total</u>	<u>\$57,400.00</u> (U.S.)
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Submitted by Dr. K. Tsuchiya, Keio University, Tokyo, Japan.