BOARD OF DIRECTORS MEETING

New York, N.Y. May 12, 1949

A luncheon and meeting of the Board of Directors of the Lead Industries Association was held on Thursday, May 12, 1949, at 12:30 P.M., at the Down Town Association, New York, N.Y.

PRESENT	REPRESENTING
Norman Hickman	The American Metal Co. Ltd.
K. C. Brownell	American Smelting & Refining Co.
J. A. Costello	Ethyl Corp.
Clarence Glass	International Smelting & Refining Co. Anaconda Sales Co., Agents
J. A. Martino	National Lead Co.
F. E. Wormser	St. Joseph Lead Co.
G. H. LeFevre	United States Smelting Refining & Mining Co. Inc.

OTHERS

W. B. Clancy	American Smelting & Refining Co.
D. A. Merson	National Lead Co.
C. M. Chapin, Jr.	St. Joseph Lead Co.

Robert L. Ziegfeld, Secretary-Treasurer

Mr. Wormser occupied the chair.

The minutes of the previous meeting of April 8, 1949, were approved.

AMENDMENT TO BY-LAWS

By letter ballot and vote in person, the following amendment to Article IV, Executive Committee, Sec. 1 of the By-Laws, which was recommended at the Board meeting on April 8, 1949, was approved:

> "Article IV, Executive Committee, Sec. 1, shall be amended to strike out "five (5)" in the first sentence and substitute therefor "six (6)."

It was decided to table the election of the sixth member of the Executive Committee for the position created by the foregoing amendment until a later meeting.

A suggestion was also made that the secretary investigate the possibility of arranging for rotation of the members of the Board and Executive Committee so that a certain number of members would be automatically retired each year and not be eligible for reelection until a certain specified period had elapsed.

ANNUAL MEETING - 1950

Plans for the 1950 annual meeting of the Lead Industries Association were discussed and it was generally felt that the secretary should try to make arrangements, at least for next year, somewhat similar to those made during 1949. It was decided that Chicago would be the best place to hold the meeting and that the secretary should work closely with the secretary of the American Zinc Institute so that members wishing to attend meetings of both organizations could do so with a minimum loss of time.

HYGIENE AND SAFETY

Educational Film on Lead Poisoning - The secretary reported further on the suggestion that it might be advantageous to make a motion picture on the diagnosis, treatment and prevention of lead poisoning for the education of medical students, medical men, health authorities and others interested. He explained that he was quite sure that the sponsorship of the American Medical Association could be enlisted and that if such a film were made, it should be with the advice of a committee of top-ranking medical authorities in the field. He reported that preliminary investigations indicated that the cost, in color, of a 30-minute film of this type would run from $35,000 to $50,000, but that black and white would probably suffice and would reduce the cost from 20 to 25 percent. He was instructed to investigate this subject further.

Research at Johns Hopkins University - The question of an additional grant to Johns Hopkins University to continue the research on antidotes for lead poisoning, under the direction of Dr. Alsoph H. Corwin, was discussed. Correspondence is attached as Exhibit "A." The secretary reported that in preliminary conference with the Research Corporation, that organization had indicated a probable willingness to subscribe half of the $5,000 fund requested if the Lead Industries Association subscribed the other half. He further explained that the $2,500 grant from the Lead Industries Association could be made from the 1949 approved budget without a subscription of additional funds.

The grant of $2,500 to be matched by a similar grant of the Research Corporation to carry on this work for another year was approved.

Research at Harvard College and Children's Hospital - The secretary made a brief report of the work conducted under a Lead Industries Association grant to Harvard College and the Children's Hospital in Boston over the past year. He stated that fifteen cases had been studied and that of these, six had been proven not

to be lead poisoning after urinalyses were made from the funds granted, already justifying the worth of the project. Four of these six had previously been diagnosed as lead poisoning by the X-ray examination. He explained that it was the desire of those conducting the work to continue it in order to provide a broader statistical background and that this could be done for one year from June 30, when the present grant expires, at a cost of $2,200. The Board approved a grant of $1,100 from the current budget, without additional subscriptions, to continue this work from July 1, to December 31, 1945, further consideration to be given later in the year as to the continuation of the work in 1950.

Research at the University of Colorado - A request for financial assistance for research on the use of strontium and pyrocatechindisulfonate as antidotes for lead poisoning from Dr. Princi of the University of Colorado (attached as Exhibit "B") was tabled.

Research by Memorial Hospital and New York State Department of Labor - An invitation to cooperate, without financial assistance, in a study of lead poisoning by the New York State Department of Labor and the Memorial Hospital, New York, was discussed. (Attached as Exhibit "C") The secretary was instructed to cooperate as far as possible with the New York State Department of Labor and the Memorial Hospital in its projected study of lead poisoning.

USEFUL INFORMATION ABOUT LEAD

The secretary reported that the work of revising the original publication of "Useful Information About Lead," published by the Association in 1931, was now about complete and reminded the Board that a reserve of $4,000 had been set aside for a new edition several years ago but that present printing costs indicated that a new edition of 10,000 copies would probably cost about $6,000. In view of this, he explained that he had discussed with the McGraw-Hill Company the possibility of the book being published by the McGraw-Hill Book Company with the Association guaranteeing to purchase a certain number of copies. Arrangements had been made to discuss this further with the McGraw-Hill Company and it was, therefore, decided to postpone any action on printing the book until a report of the conferences with the McGraw-Hill Company could be considered by the Board.

PROCEEDINGS ANNUAL MEETING - 1949

The secretary reported that the Proceedings of the Annual Meeting, held in Chicago in April, had gone to the printer and should be ready for distribution in about a week. He stated

that he proposed to distribute free copies to the entire membership mailing list of the Association and to anyone who attended the meeting if he was not on the mailing list. He requested instruction as to the general distribution of the Proceedings. It was decided that they be offered for sale at a price not to exceed $2.00, to cover the cost, the actual price to be left to the discretion of the secretary.

REINVESTMENT OF FUNDS

The secretary was instructed to reinvest the $34,000 which would be realized on maturity of the U.S. Certificates of Indebtedness in which the funds are now invested, on June 1, in new short term Certificates of Indebtedness.

RESIGNATION - GENERAL LEAD MANUFACTURING COMPANY

The secretary read a letter of resignation from the Association from the General Lead Manufacturing Company of Denver, Colo., as follows:

> "I have your statement before me for second quarter subscription.
>
> For some time, especially since the Plumbing Promotion Program has been discontinued, I have felt that we are receiving but little benefit from our membership.
>
> It is therefore with regret that we feel obligated to cancel our further membership in the Lead Industries Association, having been one of the early members and staunch supporters."

and explained that he had written the Company asking that its decision be held in abeyance on the ground that the Plumbing Promotion Program of the Association had not been discontinued but had merely been curtailed, and that a new program was to be considered sometime during the current year.

The Board decided to take no action on the resignation until a reply had been received from the General Lead Manufacturing Company.

The meeting adjourned at 2:30 P.M.

Robert L. Gregg

Secretary

Board of Directors
Meeting Minutes

Exhibit "A"
May 12, 1949

From

Manfred Bowditch

To

Mr. Ziegfeld

May 9, 1949

Subject: Summary of statement by Dr. A. H. Corwin, May 5, 1949, Development of an Antidote for Lead Poisoning

Studies in 1941 under the residue of a grant from the Rockefeller Foundation led to interest in antidotes for heavy metal poisoning through the observation that it was possible to extract mercury from biological tissues by means of the reagent "dithizone."

Financial aid from the Research Corporation enabled pursuit of this subject, leading to the determination that, while dithizone itself was not practical as an antidote, the symmetrical meta-dicarboxyl derivative, in the form of the sodium salt, had apparent possibilities. It was tried against cadmium, mercury, silver, arsenic, antimony and finally lead. The results against lead poisoning were sufficiently encouraging to warrant concentration on this metal.

Joint support by the Research Corporation and the Lead Industries Association was then secured. Chemically, efforts to develop even more water-soluble compounds were unsuccessful, but are believed to merit renewal. Biologically, using strains of pure-bred mice, these results were attained:

1. The dicarboxy dithizone antidote was shown to be no more toxic than table salt. (This is in marked contrast to BAL, British Anti-Lewisite, which was thought to give great promise as a lead antidote.)

2. By colonic irrigation, it proved very effective in controlling intestinal lead colic.

3. Evidence was adduced to justify the belief that further experimentation would demonstrate effective control of lead poisoning.

Since the termination of the R.C.-L.I.A. grant, further work by doctoral candidates has resulted in:

1. Standardization of the technique for experimental intoxication with lead.

2. Establishment of the structure of dithizone on firm ground.

3. Resolution of the debated question of the nature of the chemical bonding between heavy metal compounds and dithizone.

4. Determination of the chemistry of the poisoning and antidote reactions.

5. Doubling of yields in synthesis of the needed compounds.

Publications on two of these subjects have been prepared and a third is planned.

N 611.01

Before the outcome of this work can have the hoped-for results in the treatment of human lead poisoning, three further steps are deemed essential:

1. The yield of the synthesis must be further stepped up to accumulate a working reserve of the antidote.

2. Its efficacy on animals must be further studied.

3. Its stability in air, hitherto unsatisfactory, must be materially improved.

Doctor Corwin believes that each of these three requisites can be accomplished and asks a grant of $5000 for this purpose, $4500 for the full-time services of a skilled organic chemist for one year and $500 for chemicals and equipment

---

Supplementary:

The initial Research Corporation grant was authorized on February 3, 1944 and a total of $3995 was expended. The work was started on February 14 and continued for somewhat more than a year.

The Research Corporation-Lead Industries Association grant was authorized on January 22, 1946 in the amount of $7200. The full amount, of which each organization contributed one-half, was expended. The work was started on July 1 and continued for somewhat more than a year. U. S. Patent No. 2,441,346, which is freely available to the public, resulted.

Doctor Corwin has advised me of his belief that the work now contemplated can be completed within a one year period. He would hope to start the work on July 1 or October 1, depending on the availability of a qualified chemist.

LIA00366

DEVELOPMENT OF AN ANTIDOTE FOR LEAD POISONING

Alsoph H. Corwin
The Johns Hopkins University

I wish to present for the consideration of the Lead Industries Association a statement concerning the work which has been completed in this laboratory on the general subject of antidotes for heavy metal poisoning and a proposal for further study with the particular problem of lead poisoning as the major consideration. The program which I shall present could be carried forward most efficiently if the services of a full-time and skilled organic chemist were available for the work. We estimate that his services would require a salary of $4,500 per year and that he would require an additional $500 for chemicals and equipment during the year.

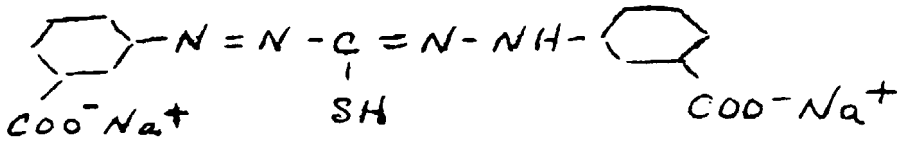
Our Early Work on Heavy Metal Poisoning

The work which will be reviewed here was performed with the collaboration of the following investigators: Dr. Lewis Sargent, Dr. Alvin Sharp, Dr. Kurt Kraus, Mrs. Martha Pelletier, Dr. James Webb, Dr. Sylvia Helm, Dr. George Jackson, Mrs. Jean Arrington, Dr. Wilhelm Frisell, Dr. John Reinheimer, and Mr. Iqbal Singh Bhatia. These collaborators have worked for periods of one to three years each on the problem at different times during its development.

In 1941 we were studying the action of heavy metals on biological systems under the residue of a grant from the Rockefeller Foundation. Our interest in the subject of antidotes for heavy metal poisoning began with the observation that it was possible to extract mercury from tissues and from organic mercurials by means of the heavy metal reagent "dithizone" without preliminary destruction of the tissues. We did not investigate this reaction quantitatively for the purpose of chemical analysis. Instead we decided to explore its possible use in the formulation of an antidote for heavy metal poisoning.

Research Corporation Grant - Cadmium Poisoning

Research Corporation extended us financial aid for the general investigation of heavy metal poisoning. We first attempted to use dithizone itself as an antidote. We soon found that it was so insoluble in body fluids that its use was impractical. We then attempted to increase its solubility and found that the symmetrical meta-dicarboxyl derivative had quite satisfactory solubility in the form of the sodium salt. It was also found that this compound had sufficient affinity for heavy metals to be of use as an antidote. The material has the following chemical formula:



The next step was the investigation of different heavy metals. We made a quick survey of toxic metals and soon found that the activity of the new antidote against cadmium was quite easily established. For this reason we concentrated our studies on cadmium poisoning for some time. We studied increased dosages, auxiliary treatments, time of successful administration and other variables.

One of the most important variables which we found was the temperature of exposure of the experimental animals, which were mice. In mice the influence of a toxic substance may be radically altered by the temperature of the animals before and during the administration of the drug and during the time of survival after the dose. We chose to control this variable rather than to abandon mice as experimental animals because of the relative cheapness of mice and because of the high degree of biological homogeneity obtainable. We do not consider statistical experimentation with dogs and other large animals to be reliable for establishing curative action unless very large samples are taken to establish both the lethal dose and the curative dose. Since each of these actions is an independent variable with genetic variation, over-all curative action is a second order variable and large numbers of experimental animals would be required to arrive at sound conclusions. With animals having great biological homogeneity, similar large numbers are not required and experimentation is relatively more rapid. In addition to this, experimentation with large animals would not have been feasible with a compound as difficult to procure as ours has been.

In addition to our work on cadmium, we worked somewhat on mercury, silver, arsenic, antimony, and finally lead. The antidote was of no value with either arsenic or antimony, as was predicted from the known lack of action of dithizone on these metals. Contradictory results were obtained on various organic mercurials. More light has now been thrown on these results by our later experimentation and we believe that the mercury field should be reinvestigated. The results against lead poisoning were encouraging and because of the interest in it as a health hazard, we decided to work further on lead poisoning.

Research Corporation - Lead Industries Association Grant

Lead Poisoning

At this time we applied for an extension of the grant from Research Corporation. They suggested a joint grant with the Lead Industries Association and this was arranged.

Our experimentation under this joint grant was of two types, chemical and biological. On the chemical side we attempted to prepare compounds of still greater water solubility. In this search we were partially successful. New compounds were found which were more soluble in water than the dicarboxy-dithizone. On the other hand, the groups necessary to obtain this increase in solubility were found to diminish the activity of the compounds. The end result of this chemical study

was a return to our original compound. We have not yet explored all the possibilities for securing more soluble compounds but we believe that information uncovered in our biological studies warrants still further investigation of the present antidote.

Experimental Lead Poisoning

On the biological side, we made numerous studies of the lethal action of lead when given in large doses both with and without antidote. We found that it was most difficult to obtain a reproducible intoxication in the laboratory with this metal. Attempts at chronic intoxication gave quite variable results and attempts at acute intoxication, while not so variable, were still far removed from the results obtainable with cadmium. Since the termination of the grant we have succeeded in standardizing the technique of experimental intoxication with lead.

The difficulty in lead intoxication is that the injection of soluble lead salts usually results in the rapid precipitation of the lead in a quite insoluble and variably toxic mass. This action can be observed best in the peritoneal cavity. Out studies show that this precipitation can be prevented by the use of a mixture of citrate and thiosulfate administered with the lead. These substances form stable lead complexes which are broken up slowly and fairly reproducibly by the body so that a reasonably predictable intoxication can be secured. Incidentally, the toxicity of lead administered in this form is several times as great as when administered as the nitrate or acetate.

Many of our early failures in the attempted use of antidotes were due to the fact that we were administering up to five times the lethal dose of lead and that the antidotes had the power to mobilizing the lead so laid down. A large amount of lead-dithizone was then thrown on the kidney for excretion and the material was not sufficiently soluble to permit its elimination. It was this observation which led us to desire more water-soluble compounds. When we had found the proper dose level for the production of actue lead poisoning in the laboratory, the picture changed and better results were obtained.

Blandness of the Dithizone Antidote

One biological finding made at this time was of the greatest importance with respect to the possible use of dicarboxy dithizone as an antidote. This was the establishment of the lack of toxic action of the proposed drug in mice. We fed mice water containing the antidote from the time of their weaning through their entire lifetimes and found that they were capable of raising normal young when given no untreated water. We established the fact that the drug is comparable in blandness to table salt. When the latter substance is given in sufficiently high concentration it causes an upset in the osmotic balance and consequent deleterious action. The antidote required a solution of similar strength to cause toxic action and it was found that this was also due to upset of the osmotic relationships. This is one of the few drugs that we have dealt

with that is to be classified as being harmless as salt and we have no hesitation in using it.

As a further example of the mildness of this drug, we have found that a two per cent solution is not irritating to the eyes. This discovery led to the use of the material in colonic irrigation.

Control of Lead Colic

Animals poisoned with lead exhibit more or less severe symptoms on intestinal colic. When the intoxication is severe, extensive capillary hemorrhage can be observed in the intestines. We have observed that the intestinal colic can be controlled very effectively by colonic irrigation with the dithizone antidote. In severe poisoning, the capillary hemorrhage is also controlled, so that colonic irrigation adds materially to the efficacy of the treatment of experimental lead poisoning.

Contrast Between BAL and Dicarboxy Dithizone

The outstanding property of BAL which is noted in experimentation with it is its revolting odor. This contrasts with the dithizone antidotes which ar odorless. BAL can be tolerated in doses of only 3 mg./kg. without discomfort. In much larger doses it causes increasingly severe psychic symptoms. Our dithizone antidote has been given parenterally at the level of 400 mg./kg./day for four weeks without perceptible physiological alteration and at the level of 2500 mg./kg./day by mouth throughout the entire life span of animals without perceptible interference with physiological functions.

BAL has not proved effective as an antidote for lead poisoning in the first trials which have been made with it. Survival times of intoxicated animals were shortened when it was administered. In our antidote tests on animals receiving what we now know to have been approximately five times the minimum lethal dose of lead, the survival times were more than doubled. Both drugs mobilize lead reserves of the animal. This appears to be the cause of the observed shortening of survival times in animals treated with BAL. The mobilization of lead to the kidney does not obscure the antidote action in the case of dicarboxy dithizone, however. On this basis we feel encouraged to believe that further experimentation with smaller doses of lead will demonstrate effective control of poisoning.

Use of Larger Animals

During this period we also did a limited amount of experimentation on larger animals but we are not in a position to draw final conclusions from it. Because of its lack of stability in solution, our antidote has to be standardized biologically. The only reliable method for doing this is to test its power as an antidote for cadmium poisoning. We were able to establish the fact that it acts as an antidote in rabbits just as it does in mice but the work lacks the precision of the mouse work

because of the smaller number of animals that we were forced to use. This arises from the difficulties encountered in preparing the antidote in larger quantities. We were not able to progress beyond the point of standardization of the antidote on cadmium with a limited number of rabbits and cannot report its effectiveness in lead poisoning in rabbits.

Later Chemical Work

Since the termination of the grant by Lead Industries Association and Research Corporation, we have succeeded in standardizing the dosage of lead for laboratory investigations, as was pointed out above, and have made extensive chemical investigations, through the medium of the work of doctoral candidates. The chemical work has been of several types, all contributing to a better understanding of the chemistry fundamental to the antidote reaction.

Our first problem was to establish the structure of dithizone with certainty. We found that most preparations are quite impure and it is possible to conclude that the yields of chemical degradation products obtained by early investigators might have stemmed from the impurities instead of from the dithizone itself. We have now established the structure of dithizone on firm ground. A publication on this subject has been submitted to the Journal of the American Chemical Society.

The next problem was to establish the nature of the chemical bonding in the compounds between heavy metals and dithizone. The literature presents no agreement on this subject. We believe that we have been able to clear up the debatable points and hope to be in a position to publish our findings in this field in the near future.

The third problem was to establish the chemistry of the poisoning reaction and of the antidote reaction on firmer ground. This has also been accomplished and a publication on this subject has been completed and is being submitted to the Journal of the American Chemical Society.

Next in order was to improve the yields in the synthesis of the necessary compounds for physiological study. We have been partially successful in this study, having doubled the yields of the compounds desired. Even this increase in yield leaves a considerable distance to go and further studies on the by-products of the dithizone reaction and their elimination are necessary before these substances will be readily available for our biological studies.

Finally, we have worked on the chemical stabilization of dithizone and its derivatives. This work has not yet yielded definitive results. New derivatives have been prepared which are quite stable chemically but which are not effective antidotes. The field has not been exhausted and there is still a good possibility of preparing derivatives that will be stable to the air and still be effective antidotes.

Future Experimentation

At the present time, the most pressing need is to make available a large quantity of our antidote for a definitive series of animal experiments. The chemical work which would be necessary would involve a series of studies on the improvement of yields in the preparation of the material with consequent accumulation of a working reserve. With this, experiments could be run on a large enough scale to make certain of the limits of efficacy of the antidote in lead poisoning.

The next most important investigation is the production of an air stable material. This would involve further work along the lines already laid down, consisting of the selective chemical reaction of the oxidizable group on the molecule to secure stabilization. We have reason to believe, from past experience with selective chemical procedures, that a method can be found for the production of the desired substances.

We should propose, then, to concentrate our research upon three lines of investigation: first, the improvement of the synthesis of our present antidote and the accumulation of a working reserve; second, the study of this material on animals to determine decisively its efficacy as an antidote; third, the possible improvement in the compound to secure a material which would be stable in the air.

(signed) Alsoph H. Corwin

May 5, 1949

Board of Directors
Meeting Minutes

Exhibit "B"
May 12, 1949

From: Manfred Bowditch

To: Mr. Ziegfeld

May 6, 1949

Subject: Dr. Princi's proposal, dated March 2, 1949

The following are condensed comments on the subject proposal, based upon extended discussions with Drs. J. C. Aub, M. H. Corwin, R. A. Kehoe and S. H. Pinto, briefer talks with Drs. R. K. Byers, T. L. Shipman, J. J. Waring and Dr. Princi himself, and my own knowledge of animal experimentation of the type outlined.

1. There is question whether both treatment and prophylaxis should have simultaneous consideration. Treatment is by far the more probably fruitful of the two.

2. There is next to no enthusiasm for strontium among the authorities, somewhat more for pyrocatechindisulfonate, but nothing approaching unanimity.

3. Should dogs be used, or mice? Again there is difference of opinion, Dr. Corwin favoring mice on the ground that strains of known susceptibility to lead are available, Dr. Kehoe voting for dogs because of their more adequate blood supply, and Dr. Aub seeing both sides. Dr. Princi is not interested unless he can use dogs.

4. Though I would question some details, I do not consider Dr. Princi's overall cost figure excessive for a single year. I am quite certain, however, that he will want to continue the work beyond that period.

5. Quite apart from the above considerations is the question of lending a hand to a new and promising laboratory. There are today all too few reliable institutions where such work can be done and the potential value to industry of a worth-while addition to the list is obvious.

6. My conclusion is that, unless we are prepared to support both the work of Dr. Corwin and that of Dr. Princi, we should chose in favor of the former. Dr. Pinto, Dr. Princi's prime supporter, is in agreement as to this.

MB

N 611.03

LIA00373

University of Colorado
Medical Center
4200 East Ninth Avenue
Denver 7, Colorado

December 31, 1948

Mr. R. L. Ziegfeld, Sec.-Treas.
Lead Industries Association
420 Lexington Avenue
New York 17, New York

Dear Mr. Ziegfeld:

For some time this laboratory has been interested in the treatment and prophylaxis of lead intoxication. We have recently been working with two substances which seem to show promise. One is Strontium and the other is Sodium pyrocatechindisulfonate. Since we are able to work on the problems only in our spare time it would naturally take years to arrive at any successful conclusions.

Dr. Sherman Pinto, of this city, has suggested that your organization might be interested in promoting research of this type. If you think that such a project is worth while and would like to have more information concerning our plans, I would be very glad to outline in detail what we propose to do, how we expect to carry it out and the approximate cost.

Mr. Manfred Bowditch of your organization is familiar with our laboratories and with some of the work which we are carrying on here, and I am certain he will be able to give you any general information you might desire.

I shall be glad to answer any questions that you might have at any time.

Very sincerely,

Frank Princi, M.D., Director
Division of Industrial Medicine

LIA0C374

N 611.04

Although lead absorptions and lead intoxications have long been recognized as serious industrial hazards, the state of knowledge concerning the treatment or prophylaxis of this condition is wholly unsatisfactory. Recent investigations have shown that none of the drugs or substances in common use in the treatment of lead absorption have any actual effect on the metabolism of lead. It is a well known fact, however, that strontium in solution at pH 7.5 to 8.0 removes lead from solution either by adsorption or absorption (in vitro). If the strontium as an ion or as the lactate molecule forms a complex with the lead ions in the blood and thus prevents deposition in the bone and facilitates excretion in the kidney or intestinal tract, then it is readily conceivable that strontium will act as a de-leading agent. If, however, the strontium removes lead from solution only by co-precipitation, adsorption or absorption, it is difficult to visualize (a) how the body would react to the presence of such insoluble material in the blood stream and (b) a mechanism by means of which undissolved material could be removed from the blood by excretion. However, other workers have found that in the serum of dogs fed strontium lactate the filterable strontium is always low and often entirely absent even when the total strontium is fairly high. Haldane reports that the toxicity of strontium varies with the species of animal, being tolerated in relatively larger amounts in humans. McCance and Widdowson found the kidney to be the main organ of excretion for strontium in human subjects. They were able to recover approximately half the injected strontium in two days, about 80% was in the urine. Feeding experiments on dogs in this laboratory have shown us that these animals can ingest considerable amounts of strontium lactate without apparent change in physical condition.

Sodium pyro Catichin, Di-sulfonate (di-catichin) is a compound which has been used in the past as an analytical reagent for the estimation of iron in micro quantities. The similarity of the di-catichin reaction with iron to BAL's reaction with mercury led Borghero in Italy to test its effects on lead. Their results were very meager and inconclusive, but showed great promise of having the same type of reaction with lead as does BAL with mercury. If this is true, di-catichin should act as a therapeutic and/or prophylactic drug for lead intoxications. Experiences in this laboratory with di-catichin have shown that it is not acutely toxic to dogs or mice; that of several heavy metals tested in vitro only iron forms a colored complex and lead a turbid solution. All others gave no reaction whatsoever.

We propose to study the therapeutic value of both strontium and di-catichin by direct animal experimentation. Five groups of dogs will be used. One group will be given lead only. One will be given lead and strontium. One group will be given lead and di-catichin. One group will be given strontium only and one group di-catichin only. By this means we hope to (1) determine any cumulative toxicity of strontium; (2) determine any cumulative toxicity of di-catichin; (3) determine whether or not strontium has any effect in preventing clinical signs and symptoms of lead poisoning and if it has any effect in removing lead from the body; (4) determine whether or not di-catichin has any effect in preventing clinical signs and symptoms of lead poisoning and if it has any effect in removing lead from the body. Most of the above items will be determined by clinical means. It is also planned to determine lead levels in the body fluids throughout the experiment on all animals.

This can be done for $5,460.00, which is distributed as follows:

Board and room for dogs for one year	$ 960.00
Animal Custodian	2400.00
Chemist (Part time)	1800.00
Supplies (chemicals, paper, notebooks, etc.)	300.00

We believe the above proposal to be worthy of your consideration. Any further questions which might arise in your mind will be answered promptly, or if you have any suggestions or criticisms of the above please communicate them to us.

Frank Princi, M.D., Director
Division of Industrial Medicine

March 2, 1949

Board of Directors
Meeting Minutes

Exhibit "C"
May 12, 1949

C O P Y

STATE OF NEW YORK

DEPARTMENT OF LABOR

Albany

NEW YORK OFFICE 80 CENTRE STREET

New York, N.Y.
Division of
Industrial Hygiene
and
Safety Standards

May 6, 1949

Mr. Manfred Bowditch
Director of Health and Safety
Lead Industries Association
420 Lexington Avenue
New York, New York

Dear Mr. Bowditch:

In line with our telephone conversation last week, I am presenting you with a brief resume of our projected lead study for consideration by the Lead Industries Association at their next meeting on May 12th.

It is, as you will see, primarily an effort to find better methods than are now available for the early detection of lead absorption or lead intoxication as an aid to prevention--methods which are also less subject to error from contamination of samples. Present inaccuracies stem largely from the fact that one is attempting to obtain accurate quantitative estimations of minute amounts of lead in blood or urine, for example, where the very substance to be measured is also the contaminant. Another objective is to obtain further data on some of the more obscure physiological and biochemical mechanisms involved.

The study will include briefly:

1) A determination of coproporphyrins in the urine, both by the usual rapid field method and a more detailed research method, in order to check the relative accuracy of the former and develop further information as to the physiological significance of this test.

2) Special studies to demonstrate abnormal physiology in red blood cells which may lead to a simple field test for evidences of early lead intoxication.

3) Selected blood chemistry determinations.

N 611.06

LIA00377

4) The usual occupational histories; physical examinations; hematological studies including stipple cell count and basophile aggregation tests; and chemical estimations of the lead content of blood and urine by standard methods.

5) Air lead determinations to evaluate the exposure of the workers under study.

In order to properly evaluate the significance and usefulness of the newer procedures contemplated, we believe it will be necessary to carefully correlate all such findings with the more familiar laboratory and clinical data now available with reference to lead absorption, lead poisoning and lead exposure. For that reason, we propose to include the conventional studies listed under 4).

We believe we are fortunate in having the cooperation of the Memorial Hospital in New York City in connection with the coproporphyrin determinations. First, they have a metabolism research laboratory which is working full time on porphyrins in relation to cancer; and they are using chemical methods which are quantitatively far more accurate than anything in use elsewhere either here or abroad. Since ether extraction is a necessary part of their method and the quantities of ether necessary are large, no industrial hygiene or public health laboratory could possibly take on the potential explosion hazard involved in its use. Furthermore, it will be an opportunity for us to contribute to cancer research in providing Memorial Hospital with data on workers exposed to lead for comparison with all of their other data on a large variety of cancer patients.

It seems to us that this is a golden opportunity for a scientific study in which the Lead Industries Association could also participate. In so doing, they would be making a contribution to a better scientific understanding of lead poisoning, which is one of their important objectives, as I understand it. Needless to say, their cooperation would greatly simplify our problem of getting the necessary series of lead workers for the study, and we would appreciate this assistance greatly.

If you were not personally connected with the Lead Industries Association at this time, it would probably not have occurred to us to suggest this as a cooperative project. But I think you will agree with me that it is worthy of consideration.

If any questions arise which I can clarify, please let me know.

Very sincerely yours,

s/ May R. Mayers

t/ May R. Mayers, M.D.
Chief, Medical Unit

MRM:MK