

INTERNATIONAL LEAD ZINC RESEARCH ORGANIZATION

888 MADISON AVENUE, NEW YORK 17, N. Y. ORG-ON 8-9080

SCHRADE F. RADTKE
DIRECTOR

September 24, 1964

To Members of the LIA-ILZPO Health and Safety Committee:

Subject: 1965 Research Budget - Proposals and
Work Statements for Consideration at
the 1965 Budget Meeting

Attached is the 1965 Catalog of Health and Safety Research for your review in preparation for the Health and Safety Committee Budget Meeting to be held October 15, 1964, at the Lead Industries Association's Conference Room, 14th floor, 292 Madison Avenue, New York, N. Y., at 9:15 A. M.

This material is designed to be used as a guide in our discussions and contains, besides a list of items to be discussed, review and comments on past performance of some of the projects.

Also attached are copies of two project proposals to be discussed and voted on at the meeting. There will be other projects for our consideration which you will receive at the meeting as they have not yet been submitted to this office. This is the reason why the dollar figures in the Catalog are incomplete.

Please review these items carefully and be prepared to make your decisions at our meeting so that our recommendations may be completed at that time. We suggest that you bring the Catalog to the meeting to serve as reference.

Very truly yours,

Don G. Fowler

Don G. Fowler, Secretary
Health and Safety Committee

DNF:md
cc: Chemical Subcommittee
Technical Steering Committee
Enc.: Catalog
LH-75
ULM-14

1965

CATALOG OF HEALTH AND SAFETY
RESEARCH - LEAD

LIA-11270
HEALTH AND SAFETY COMMITTEE

- I. Review of Existing Projects
and Extension Proposals
- II. Work Statements
- III. Extension Proposals

1965 Catalog of Health and Safety Research - Lead

I. REVIEW OF EXISTING PROJECTS AND EXTENSION PROPOSALSLH-75 - Human Exposure to Particulate Lead Compounds in the Air Under Experimental Conditions -- The Kettering Laboratory

Progress on this project is on schedule and we are asking for a one-year continuation at this time. Our needs will be satisfied when the Kettering Laboratory has developed guidelines on the amount of lead that will be safe in urban atmospheres, which guidelines will be made available to government agencies upon request.

Budget Recommendation \$35,000

LH-86 - Lead Glazes for Dinnerware - Rutgers University

Listed for information purposes only. The money was appropriated in 1964.

Amount Appropriated \$6,977

LH-76 - The Testing of Organolead Compounds for Possible Endocrinological and Anti-Hammary Tumor Activity - The Worcester Foundation

With two organolead compounds already showing excellent promise in anti-inflammatory activity this project has made good progress. Work will continue in further exploration of promising compounds that already have been screened together with new compounds to be obtained from the Hattick and TNO Laboratories.

Budget Recommendation \$

LH-79 - Toxicity Testing for Organolead Compounds - The Nine Laboratories, Inc. and Industrial Bio-Test Laboratories, Inc.

Listed for information purposes only. Organolead compounds to be tested only as the need arises. No new funds needed. Money was appropriated in 1964.

Amount Appropriated \$10,000

1965 Catalog of Health and Safety Research - Lead

II WORK STATEMENTS

ULH-14 -- The Radioprotective Effects of Inorganic Lead
(Prepared by the New York Medical College)

ULH-15 -- Toxicity Study of Ingested Paint Film
(Submitted by Hazelton Laboratories)

III EXTENSION PROPOSALS

LH-75 -- Human Exposure to Particulate Lead Compounds in the Air Under
Experimental Conditions -- The Kettering Laboratory

LH-76 -- The Testing of Organolead Compounds for Possible Endocrinological
and Anti-Mammary Tumor Activity -- The Worcester Foundation

PART IPROJECTS FOR CONSIDERATION AT THE
LEAD HEALTH AND SAFETY COMMITTEE
1965 BUDGET MEETING

Project	Title and Contractor	Funds		Decision	
		Requested	Approved	For	Against
LH-94	A Biochemical Approach to Lead Toxicity -- Harvard Medical School				
TOTAL					

PART IIWORK STATEMENTS FOR CONSIDERATION AT THE
LEAD HEALTH AND SAFETY COMMITTEE
1965 BUDGET MEETING

Work Statement	Title	Funds		Decision	
		Requested	Approved	For	Against
ULH-14	The Radioprotective Effects of Inorganic Lead	\$ 10,054			
ULH-15	Toxicity Study of Ingested Paint Film	\$			
TOTAL					

PART III

EXTENSION PROPOSALS FOR CONSIDERATION AT THE
LEAD HEALTH AND SAFETY COMMITTEE
1965 BUDGET MEETING

Project	Title and Contractor	Funds		Decision	
		Requested	Approved	For	Against
LR-75	Human Exposure to Particulate Lead Compounds in the Air Under Experimental Conditions -- Kettering Laboratory	\$35,000			
LR-76	The Testing of Organo-Lead Compounds for Possible Endocrinological and Anti-Mammary Tumor Activity -- The Worcester Foundation	\$			
TOTAL					

Title of Project:

ULR-14

THE RADIOPROTECTIVE EFFECTS OF INORGANIC
LEAD

SPECIFIC AIMS:

Chemical agents utilized in the radiation protection of tissues, organs and whole animals vary as to structure, mode of action and species studied. Trace metals play a vital role as intracellular co-factors. Zinc, cobalt, iron, magnesium, manganese and copper are some of the metallic ions with established functions in various enzyme and transport systems.¹ Not well understood is the high concentration of cadmium in the renal cortex and the relationship of selenium² to muscle metabolism. It is conceivable that in the complex, inter-related systems that control cell function, radiation induces rapid ionization, formation of free radicals and disrupts molecular spatial arrangements. In such situations the various metallic ions would undergo severe alterations in their valence shells. The possible introduction of appropriate ions to stabilize the early changes produced by radiation is worthy of study.

This laboratory has an unusual competence in cytochemistry and histochemistry. In addition, a major group of investigators are studying the structure and function of the cardiovascular system. These include:

	Field	Formerly
Dr. Sara Schiller	Biochemistry	University of Chicago
Dr. William Outstein	Biophysics	New York University
Dr. Ralph Strebel	Exp. Path.	Institute of Research, University of Montreal (Dr. Selye)
Dr. S. Mohos	Exp. Path.	Downstate Medical Center, N.Y.
Harold Appleton, M.S.	Clinical Chemistry	National Institute of Health
Dr. Bernard Wagner	Exp. Path.	University of Washington

Working with this group on a part-time basis is an electronics expert and a physicist.

The tissues from the animals in the various experimental groups will be prepared by special techniques developed in this laboratory to evaluate intracellular, extracellular and vascular changes. Vascular changes include fixation for observations of constriction or dilatation. 3-6

Preliminary studies employing inorganic, ionized lead in the intact animal has indicated that the vascular changes consequent to lethal whole-body X-irradiation may be modified. The purpose of this investigation is to explore in detail the following questions:

1. Radiation projection of lead as a function of dose, time and tissue levels.
2. Influence of animal age, sex and diet.
3. Mechanisms of protection at a histochemical, cytological level.
4. Blood and urine changes during experiments.

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METHODS:Experiment I

Validity of Previous Observations

Group	IA	Pb(Ac) ₂	200 mg/kg	6 rats	400 r
	IB	NaCl	200 mg/kg	6 rats	400 r
	IC	Pb(Ac) ₂	200 mg/kg	6 rats	400 r *
	ID	Pb(Ac) ₂	250 mg/kg	6 rats	400 r
	IE	Pb(Ac) ₂	250 mg/kg	6 rats	400 r *
	IF	AgNO ₃	200 mg/kg	6 rats	400 r
	IG	AgNO ₃	250 mg/kg	6 rats	400 r

Note: Doses 50 mg/kg/day. X-ray: 24 hrs. after last dose except Groups IC and IE where irradiation precedes salt administration. Group IB is a sham treated radiation exposure control. Wistar rats 100 gms.

Experiment II

Effect of Dose and Time

Days	1	2	3	4	5	7	10	14	21
Group 2A (6)	+	+	+	-	+	R	-	-	-
2B (6)	+	+	-	+	R	+	-	-	-
2C (6)	+	-	+	+	+	-	R	-	-
2D (6)	+	+	-	-	+	-	+	R	-
2E (6)	+	-	-	-	+	-	+	+	R
2F (6)	+	+	+	-	-	R	+	-	-

+ 50 mg Pb (Ac)₂ 1.P.
 - No injection
 R 400 r X-ray

The experimental design is to relate dose schedule as a fixed variable to time. In each group of 6 animals there are 3 males and 3 females of 100 gms. initial weight. Note that Group 2B and 2F will receive Pb in the post-irradiation period.

Experiment III

Enhanced Diet Study

Repeat of Experiment I with the following exceptions	
Group III-IA	Ad libitum diet
III-ID	Enriched protein diet 25% including 8% amino acids
III-IF	Ad lib
III-IG	Enriched

The 8% rich amino acids will be administered by gavage and will constitute a 25% inc. in protein N over the standard daily consumption of food.

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Throughout all experiments, blood and urine samples will be obtained at judicious intervals for the following determinations:

BLOOD

Hemoglobin
Hematocrit
Peripheral WBC and differential
Ks, K, Ca, electropherogram
Lead
B U N

URINE

Lead
Proteins
Casts
Cells, Sp. Gravity

Tissues obtained at autopsy will include:

Brain, Lungs, Heart, Liver, Spleen, Stomach, Kidneys, Adrenals,
Gonads, Skin, Bone, Bone Marrow.

In addition to routine staining, where indicated the following histochemical reactions will be analyzed.

1. Oxidative enzymes
2. Phosphatases
3. Basic proteins
4. Connective tissue polysaccharides

The experiments will be modified during the course of the investigation at the discretion of the investigators. Promising leads will be followed at no additional expense. The experimental design will yield statistically significant information which will answer in large part the original problem listed under title of project. The project will require 6-8 months for completion.

CURRICULUM VITAE

Bernard M. Wagner, M. D. - Professor and Chairman, Dept. of Pathology
(Princ. Invest.)

Ralph Strebel, Ph.D. Assistant Professor of Experimental Pathology
Lillian Bedell, B.A. Chief, Histochemistry Laboratory

FACILITIES AVAILABLE

Animal Facilities
Histochemistry Laboratory
Cytochemistry Laboratory
Histopathology Laboratory
X-ray machine (supervoltage available)

REFERENCES:

1. Enzymes: Dixon, M. and Webb, E.C., Academic Press Inc., New York, 1958
2. Schubert, J.R., Muth, O.H., Oldfield, J.E. and Remmert, L.F.: Experimental Results with Selenium in White Muscle Disease of Lambs and Calves, Fed. Proc., 20: 609, 1961
3. Wagner, B.M.: Studies of Vasoconstriction, Bull. N.Y. Academy of Medicine, 38: 66, 1962
4. Van Citters, R., Wagner, B. M. and Rushmer, R.: Architecture of Small Arteries during Vasoconstriction, Circ. Res., 10: 668, 1962.

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5. Van Citters, R., Wagner, B.M. and Rushmer, R.: Arterial Walls during Vasoconstriction, Cor et Vasa, 1:4, 1962 (text in Russian)
6. Wagner, B.M.: Aleutian Disease of Mink, Arthritis and Rheumatism, August, 1963

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BUDGETPERSONNEL

Principal Investigator - Dr. B. Wagner	-----
Co-Investigator - Dr. Ralph Strebel	3,000
Technician, part-time	2,500
Animal Care-taker, part-time	1,140

EQUIPMENT

NONE	-----
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CONSUMABLE SUPPLIES

Animals - Wistar Rats (100) - Animal Food, bedding	200
Histochemical reagents, supplies	1,000
Histology supplies	300
Blood and Urine tests	500

OTHER EXPENSES

X-ray technician, part-time and use of equipment	200
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TOTAL DIRECT EXPENSES	\$9,140
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Overhead 10%	914	\$10,054
		TOTAL