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PROPOSED RESEARCH PROGRAM AND BUDGET (U)

July 1, 1947 - July 1, 1948

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Submitted by:

Andrew H. Dowdy, M. D.,
Professor of Radiology, The University of Rochester
and
Director, Rochester Project, Atomic Energy Commission

[redacted]

1152008

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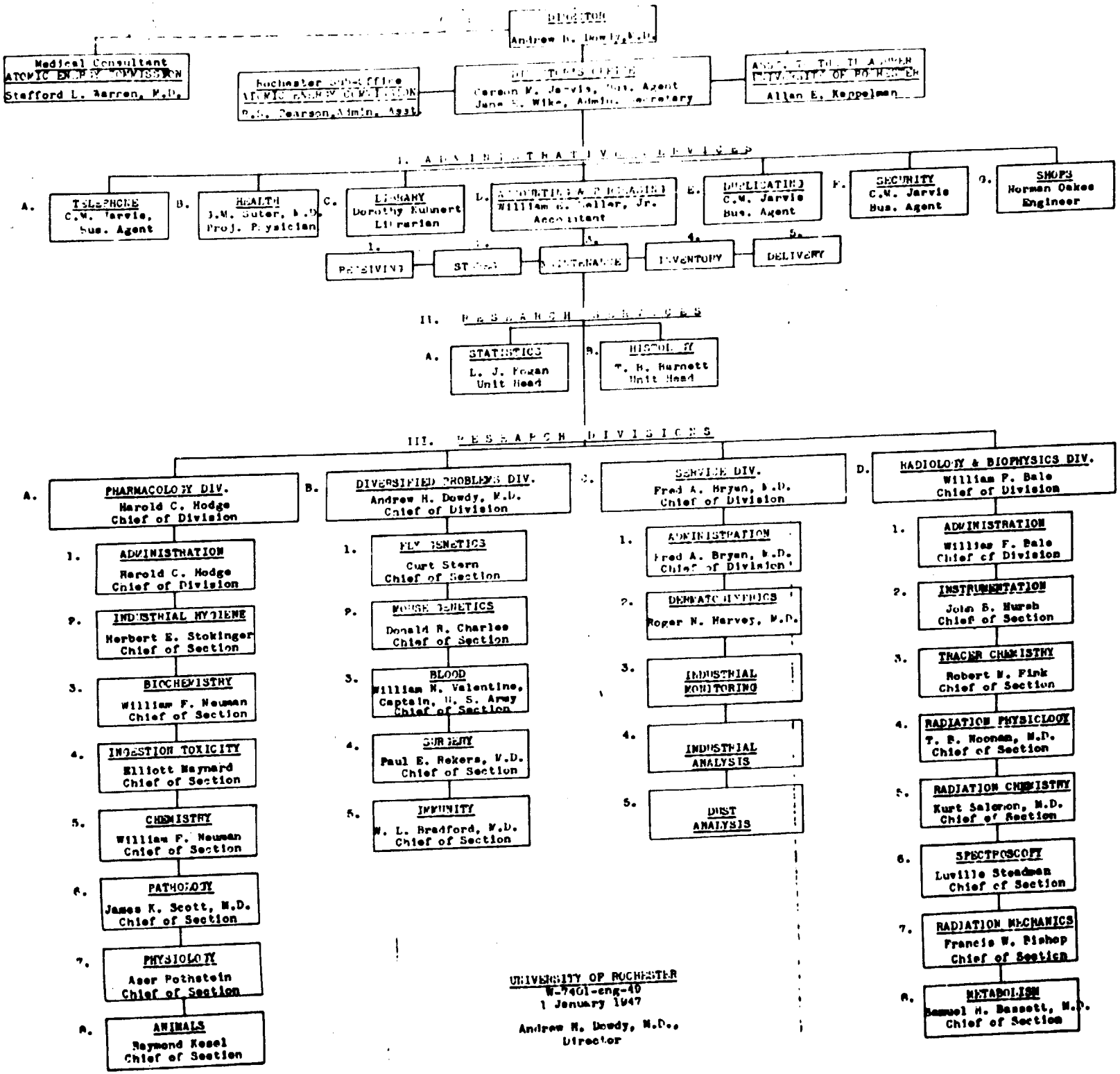

UNIVERSITY OF ROCHESTER
W-7401-eng-49
1 January 1947

Andrew H. Dowdy, M.D.,
Director

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II.

INTRODUCTION

A. PHARMACOLOGY AND TOXICOLOGY DIVISION:

The function of this Division is to determine the toxicity and pharmacology of the non-radioactive chemicals and compounds of interest to the Atomic Energy Commission during the course of production and utilization of atomic power and related products. Such an undertaking necessitates an extensive biological program supported by intensive studies into the chemical and physical properties of the various compounds, their mode of action, distribution, and storage in the body, and their mode and rate of elimination from the body. A fundamental understanding of these mechanisms of action is imperative if intelligent prophylactic and therapeutic measures are to be developed.

B. DIVERSIFIED PROBLEMS DIVISION:

This Division coordinates the activities of various semi-related groups of investigators throughout the University covering the broader fields of biology and medicine. The objectives here are two-fold: (a) to obtain fundamental information and techniques appropriate to a better understanding of the effects of and mechanism of action of ionizing radiations upon various biological systems; and (b) to stimulate a broader interest by capable investigators in the field of atomic energy. Fields of interest involved are genetics, human metabolism of radioactive substances (iodine, etc.), and the effects of radiation upon immunity, protein metabolism, the hematopoietic and reproductive systems.

1152012

C. SERVICE DIVISION:

It is the responsibility of this Division to coordinate the various service functions which the Rochester Project renders to the various production centers at the request of the Atomic Energy Commission. These services include special surveys in plants relative to chemical and radiation hazards, support of a branch office for this area for the Medical Adviser to the Atomic Energy Commission, measurements relative to health physics, and special services and tests pertaining to medico-legal problems.

D. RADIOLOGY AND BIOPHYSICS DIVISION:

To this Division is delegated the responsibility for the study of all radiation hazards which may arise from the production and utilization of atomic energy. In addition to a productive research program, this Division is called upon to make surveys of various radiation hazards, pertaining to certain industrial procedures in plants, and to make appropriate recommendations. The biological program involved includes the mechanism of action of ionizing radiations and the metabolism of various radioactive elements in animals and humans. Basic information is sought relative to the distribution, storage, and elimination of the various radioactive products from biological systems. Methods for the detecting and treatment of radiation injury is of paramount importance. An active electronics and instrumentation section facilitates the functions of this Division.

1152013

III.

DIVISIONAL RESEARCH PROGRAMS AND BUDGETS

A. PHARMACOLOGY AND TOXICOLOGY DIVISION:

Chief of Division: Harold C. Hodge, Professor of Pharmacology, The University of Rochester

1. ADMINISTRATION (3201):

3201-Ad: Adsorption Studies on Bone -- (Fundamental Research) -- To study the magnitude of the deposition of various metals such as uranium, beryllium, calcium, and non-metals such as phosphates and fluorides in bone. Attempts to elucidate the mechanism of bone deposition.

2. INDUSTRIAL HYGIENE (3210):

3210-1: Dust Inhalation Studies -- At present three materials are the prime interest to the Atomic Energy Commission; beryllium, thorium, and uranium. Accordingly, the entire Industrial Hygiene Program of this area has centered its attention on the large-scale exposure of animals to these three important substances. To this end, two beryllium exposure chambers and one chamber each for thorium and uranium are planned for operation during the current fiscal year. These chambers are designed to yield approximately 28 studies.

3210-1a: Beryllium Dust Inhalation Studies:

(Project #172)-- Two-week, High Concentration Dust Exposure - 6 Studies, 6 Months.

(Project #173)-- Sixty-day, Low Concentration Dust Exposure - 2 Studies, 4 Months.

1152014

(Project #174)-- "Flood Concentration Exposure Studies - 5 Studies, 4 Months.

3210-1b: Thorium Dust Inhalation Studies:

(Project #175)-- Acute Thorium Dust Exposures - 2 Studies, 6 Months.

(Project #176)-- Acute Thorium Dust Exposures - Insoluble Dust, 2 Studies, 6 Months.

3210-1c: Effect of Particle-Size on Uranium Toxicity, 6 Studies, 1 Year: Thirty-day inhalation studies of uranium dusts of graded particle size.

3210-2: Dust Particle-Size Studies -- Toxic response is a function of the physical as well as the chemical nature of the inhaled dust. Precise information is required to evaluate the industrial hazards and to provide laboratory control of inhalation studies.

3210-2a: Sampling and Measurement of Beryllium, Thorium, and Uranium Dusts -- Annual Basis.

3210-2b: Alveolar and Nasal Retention -- Intratracheal Studies -- Preliminary Beryllium and Thorium Information.

3210-2c: Industrial Dust Survey Laboratory.

3210-3: Special Problems in Toxicology -- Requests received by the Rochester Area for experimental data vary widely from brief exposure studies on a single material to cutaneous and ocular toxicities and short-term exposures on several related materials. No foreknowledge of the number

of annual requests is possible. There are indications, however, that requests for work on the following subject will be submitted in the near future, "Toxicity of the Pyrolysis Products of C-716 and 816 Materials". Other requests are expected. Associated with materials, related to the production of atomic energy, is that of fluorine, hydrogen fluoride, and fluorides of the particular materials involved. It is anticipated that requests for toxicological work related to this element will also be received.

3210-3a: Toxicity of Special Materials -- Annual Basis

3210-3b: Fluoride Toxicity Studies Related to Beryllium and Uranium Industries

3210-4: Fundamental Research in Problems Related to Industrial Toxicology -- The following four problems have been selected as suitable for fundamental research by the Industrial Hygiene Section during the fiscal year 1947-1948:

3210-4a: Action of Uranium on Living Cells -- The Role of Lipids in Uranium Poisoning.

3210-4b: Nature of Beryllium Poisoning -- To establish the role of secondary factors in beryllium poisoning and to establish whether these factors are specific or nonspecific.

3210-4c: Physical Properties of Dusts -- To determine factors influencing (1) the stability of dusty atmospheres, and (2) separation of suspended materials from such atmospheres.

3210-4d: Properties of Living Membranes -- To study

1152016

renal dysfunction by direct methods resulting from action of poisoning by uranium and other metals; to study isolated living membranes; and to study model membrane systems.

3210-5: Engineering Laboratory -- To set up adequate engineering laboratory facilities sufficient for two chemical engineers and equipment; for work involving beryllium, thorium, and uranium dusts, and for tests of special materials.

3. BIOCHEMISTRY (3220):

3220-1: Deposition of Project Materials in Bone -- To obtain information on the deposition of project material in bone.

3220-2: Skin and Eye Toxicity of Project Materials -- To determine the approximate toxicity of project materials to skin and eye.

3220-3: Electronics Research and Development -- To provide facilities and information relative to the development of special equipment for the entire Pharmacology Division.

3220-4: The Use of Isotopes in Toxicity Studies and Fundamental Research -- To provide a central laboratory for integrating isotope studies.

4. INGESTION TOXICITY (3230):

3230-1a: Tolerance by feeding increasing doses of uranium to dogs -- To establish amount and mode of tolerance to uranium poisoning.

1152017

3230-1b: (Project #179) Acute and pilot studies, intraperitoneal and oral, of various Be compounds in Rats, mice, rabbits, and guinea -- To complete work started in 1946-47 of establishing LD50's and 90-day toxicity by feeding.

(Project #180) Chronic ingestion-toxicity studies with four Be compounds for 2 years in rats and 1 year (or longer) in dogs -- To establish toxic effects of continuous ingestion of Be compounds over a long period of time.

(Project #181) Studies of the effect of debilitation in Be poisoning -- To investigate the possibility of a debilitating factor in Be poisoning.

3230-1c: (Project #182) Acute and pilot studies, intraperitoneal and oral, of various thorium compounds in rats, mice, rabbits, and guinea pigs -- To complete work started in 1946-47 of establishing LD50's and 90-day toxicity by feeding.

(Project #183) Chronic ingestion-toxicity studies with two thorium compounds for 2 years in rats and 1 year (or longer) in dogs -- To establish toxic effects of continuous ingestion of thorium compounds over a long period of time.

3230-2: Effect of age on toxicity of beryllium and thorium -- To determine the most resistant age of rats to toxicity of beryllium and thorium.

3230-3: Rat Breeding Colony -- It is intended to maintain our rat breeding colony in order to supply rats for the entire Rochester Project.

1152018

5. ANALYTICAL CHEMISTRY (3240):

3240-1: Methods Development -- To develop analytical procedures for project materials.

3240-2: Physical Chemistry -- To provide accurate information on the properties of project materials in solutions approximating physiological conditions.

3240-3: Fluoride Laboratory -- To provide methods and analyses of materials for fluoride content.

3240-4: Routine Metals Microanalysis -- To provide accurate analyses of solutions and tissues for all sections of the Pharmacology Division.

3240-5: Routine Biochemical Analysis -- To provide the common analyses of tissues and fluids for biochemical constituents: NPN, glucose, urinary protein, etc. for all sections of the Pharmacology Division.

6. PATHOLOGY (3250):

3250-1: Anatomical Diagnosis -- A knowledge of changes brought about in the organs and tissues by different compounds is of importance in the understanding of their toxicities. Such information is often of great importance in determining the levels that may cause injury to the cells but not kill the animals.

3250-1a: Examination of Animals Exposed to Uranium, Thorium, and Beryllium.

1152019

3250-1b: Pathological Effects of Special Materials (particularly the halogenated hydrocarbons.)

3250-2: Intravenous Toxicity of Beryllium and Thorium Compounds —

1. To produce some information concerning the relative toxicity of different beryllium and thorium compounds.

2. To supply information concerning the organs or tissues most susceptible to beryllium and thorium when there is a relatively complete distribution throughout the body.

3. To determine if all beryllium and thorium compounds have a common action or if other parts of the molecule may modify its actions.

4. Information of this type should be of some value in the later studies of mechanism of action, distribution, and excretion.

3250-3: Criteria of Beryllium and Thorium Poisoning — The information already gained from a few experiments indicates that the liver is the principal organ affected following intravenous injection of beryllium compounds. The liver damage is quite severe and consists of a widespread central necrosis. The animals become jaundiced. If beryllium acts like other liver poisons, there should be a fairly wide range between the minimal lethal dose and the minimal dose that will cause liver necrosis. Because of this, it would seem evident that a test of liver function which is most sensitive for this type of damage would be of importance in giving an indication of toxicity in non-fatal levels. There is injury to lymphoid tissue and the bone marrow when large doses of beryllium are given. This may not be of importance with small sub-lethal doses, but should be investigated. A detailed thorium program will be planned as soon as further information concerning its toxicity is known.

1152020

3250-4: Tolerance to Beryllium and Thorium Compounds -- To determine whether or not animals become more susceptible or tolerant to soluble beryllium compounds when these compounds are given intravenously. Since beryllium seems to act primarily as a liver poison producing liver necrosis, one would expect the animals to become more susceptible rather than tolerant.

3250-5: Osteosclerosis in Beryllium Poisoning (Fundamental Research) -- To study the changes in calcium and phosphorus metabolism occurring in beryllium osteosclerosis.

7. PHYSIOLOGY (3260):

3260-1: Development of Lung Function Tests -- Some of the materials (such as beryllium) used in experimental inhalation studies cause rather severe lung damage. Three possible methods will be investigated: (1) Permeability of the alveolar membrane to gases by use of radioisotopes; (2) Pneumotachograms (tracings of air movements during breathing); (3) Rate of oxygenation of blood after anoxia due to O_2 lack.

3260-2: General Physiological Studies (Action of uranium, beryllium, and thorium, and other substances on isolated cells and tissue) -- The elucidation of the mechanism of action of toxic agents on higher organisms is usually difficult because of the complex interactions of various cells and tissues. It has usually proved profitable to use isolated cells and tissues for experimental material, thus avoiding many of the difficulties. One example in this laboratory has been the use of yeast cells to

1152021

investigate the action of uranium on the cell membrane. Many other examples can be found in the literature. Each toxic agent involves a different problem and requires the selection of the cells or tissues which will give the most satisfactory data. Yeast has been useful for uranium studies and will probably also be useful for thorium. Frog heart may be valuable in the study of the action of beryllium. Other tissues which are useful for experimental purposes include: phagocytes, proteses, tissue cultures, isolated muscle, sperm, eggs, etc. It is impossible to predict at the present time the most useful lines of approach for each material.

3260-3: Role of the Cell Membrane in Metabolism (Fundamental Research) -- Although considerable work has been done concerning the permeability of the cell membrane and also concerning its structure, we actually know little of its role in metabolism except that it is a barrier to passage of materials into and out of the cell. It seems highly probable that the membrane takes an active part in metabolism, particularly in relation to phosphorylation. Because the cell membrane is the first living structure to come in contact with any toxic agent, and because phosphorylating enzymes appear to be important in uranium toxic effects, the study of membranes in uranium poisoning should be investigated more fully. The role of the yeast-cell membrane in phosphorylation and dephosphorylation will be studied by use of radio-phosphate in various compounds such as adenylic acid and adenylpyrophosphates. Uranium and other metals may be useful tools in this study because they seem to inhibit phosphorylation at the cell membrane.

1152022

BUDGET

PHARMACOLOGY AND TOXICOLOGY DIVISION

July 1, 1947 - July 1, 1948

Code	Section	No.	Personnel Salaries	Materials & Supplies	Equipment	Total
3201	Administration	3	$ 14,000	$ 2,000	—	$ 16,000
3210	Industrial Hygiene	33	86,470	12,420	$ 6,000	104,890
3220	Biochemistry	13	39,000	4,500	1,500	45,000
3230	Ingestion Toxicity	15	34,710	12,690	2,500	49,900
3240	Analytical Chemistry	20	53,700	4,800	1,500	60,000
3250	Pathology	6½	20,000	13,200	1,200	34,400
3260	Physiology	6	17,900	900	1,200	20,000
	TOTAL	96½	$265,780	$50,510	$13,900	$330,190

1152023

B. DIVERSIFIED PROBLEMS DIVISION:

Chief of Division: Andrew H. Dowdy, M.D., Professor of Radiology, The University of Rochester

1. FLY GENETICS (3410):

3410-1: Genetic Effects of Low Dosage Irradiation -- To determine the effect of short-wave radiation at low dosages and rates on the frequency of hereditary changes of genes and chromosomes in germ cells of the *Drosophila* fly.

2. MOUSE GENETICS (3420):

3420-1: A Study to Determine the Period at Which Zygotes Die -- Five semi-steriles and several sex-linked lethals will be tested. The proposed study will be a continuation of the work done from 1943 to 1946.

3420-2: A Study to Determine the Number of Chromosomal Translocations in Order to Better Understand the Effects of General Body Irradiation Upon the Hematopoietic System.

3420-3: A Study of Testes and Bone Marrow to Determine the Frequency of Chromosome Damage at Various Doses and Relating that Frequency, if possible, to the Change in Rate of Cell Output.

3420-4: Breeding Tests of Suspected Gene and Chromosome Mutations in the Sperm of Irradiated Male Mice -- A continuation of the study begun in 1944.

1152024

3. BLOOD (3430):

3430-1: Effects of Irradiation on the Hematopoietic System — To study the disturbances in physiology accompanying radiation.

3430-2: Effects of Adrenal Cortical Extract and Radiation on Output of Thoracic Duct Lymphocytes and on the Titer of Lymph in Immunized Animals.

3430-2a: Observations on the effect of adrenal cortex extract on the output of thoracic duct lymphocytes in the normal cat, the thoracic duct being cannulated and adrenal cortical extract administered after obtaining a suitable baseline.

3430-2b: Experiments similar to 3430-2a except using adrenalectomized cats.

3430-2c: Effect of radiation in varying amounts on the output of thoracic duct lymphocytes in the normal cat, the radiation being given during the actual period of cannulation after obtaining a suitable baseline.

3430-2d: Experiments identical to 3430-2c except using adrenalectomized animals.

3430-2e: Observations on the comparative titers of cell free and cell rich lymph in immunized animals. This group of experiments is designed to give evidence for or against the presence of antibody globulin in lymphocytes.

3430-2f: Observations on the comparative titer of cell free lymph from the same animal (a) before and after the administration of adrenal cortical extract, and (b) before and after radiation in varying amounts.

3430-2g: Electrophoretic studies on cell free and cell rich lymph to ascertain whether significant amounts of gamma globulin are present in the lymphocytes.

1152025

3430-3: Blood Histamine Studies -- To substantiate previous investigations that in man the majority of the blood histamine is normally bound to the myeloid leukocyte.

3430-4: Observations on the Life Span of the Leukocyte.

3430-5: The Treatment of Radiation Leukopenias with Folic Acid.

4. SURGERY (3440):

3440-1: Tissue Transplantation.

3440-1a: Transplantation of normal homologous embryonal bone marrow intravenously and to specific extramedullary sites into normal and total body radiated recipients.

3440-1b: Transplantation of normal heterologous (human and bovine) embryonal bone marrow intravenously and to specific extramedullary sites into normal and total body radiated recipients.

3440-1c: Transplantation of normal homologous embryonal lymphoid or splenic tissue intravenously and to specific extra lymphoid sites into normal and total body radiated recipients.

3440-1d: Transplantation of normal heterologous (human and bovine) embryonal lymphoid or splenic tissue intravenously and to specific extra lymphoid sites into normal and total body radiated recipients.

3440-1e: Transplantation of normal homologous, adult lymphocytes and lymph fluid into total body radiated recipients.

3440-2: Evaluation of Bone Marrow Reserve and Its Effect on Radiation Intoxication.

115202b

3440-3: Effects of Rutin (a crystalline glucoside of quercetin supposed to regulate capillary permeability) on Radiation Intoxication.

3440-4: Cultivation of the Hematopoietic Tissues of Embryos and the Effect of Radiation on these Cultures.

3440-5: Fundamental Research

3440-5a: Thyroid Function as measured by tissue iodine concentration and blood iodine concentration.

3440-5b: Relationship of thyroid function or dysfunction to other hormones and enzymes such as thyroxin, phosphatase, estrogens, etc.

5. IMMUNITY (3450):

3450-1: A Study of the Effect of X-ray and Radioactive Phosphorus on the Lymphocytosis in Experimental Murine Pertussis -- This problem is designed to evaluate the effect of radiation upon immunity. Such a problem should augment basic information relative to the mechanism of ionizing radiations upon various biological systems. Investigators in charge of this problem have had long years of experience with immunity in pertussis. Additional information will be gained in correlation with this subject; namely, the improvement of the antigenic qualities of whooping cough vaccine, and a better understanding of the production of experimental bronchiectasis following whooping cough. These last two problems, which seem on the surface to have very little to do with the work of the Atomic Energy Commission, seem worthy of support in order to gain information which the Commission does desire relative to the effects of radiations upon the human body.

1152027

6. PROTEIN METABOLISM (3460):

3460-1: Effect of Irradiation on Protein Metabolism -- Total body irradiation and local body irradiation undoubtedly bring about a change in protein metabolism as manifested by nitrogen balance. It is planned to carry out radiation studies on both normal and tumor-bearing animals with subsequent studies of the nitrogen balance. Should the animal experiments give important leads, investigation will be carried to studies of the nitrogen balances in human patients having malignant diseases and receiving therapeutic doses of radiation. The design of this program as set up will not only give valuable information relative to the effect of irradiation on protein metabolism but might also throw some light on the cancer problem as a whole.

7. THEORETICAL PROBLEMS (3470):

3470-1: The Chemical Action of Irradiations (Theoretical Considerations) -- This problem consists of (a) theoretical deductions relative to possible chemical alterations from radiations having various energy levels; (b) mathematical computations with a selection of reactions which will most probably occur in any given circumstance, and (c) laboratory confirmation of these theoretical considerations.

8. HISTOLOGICAL SERVICE (3480):

The histological laboratory operating under this section is set

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up to provide routine sectioning and staining of pathological specimens, to prepare and interpret slides, to prepare paraffin specimen blocks, and to maintain centralized storage facilities for pathological sections and readings. The laboratory operates as a service unit to all divisions on the project and is completely separate from the Pathology Section of the Pharmacology Division.

9. STATISTICAL SERVICE (3490):

The Statistical Service also operates as a service unit to all divisions on the Project and is organized by the Project for the purpose of performing various types of analyses utilizing the International Business Machine and calculator installations. The Service is set up to provide speedy computation by "punched card" methods of large numbers of basic statistical values (means, medians, standard deviations, correlations, etc.) In addition to the tabulation and calculation of frequency distributions, means, standard deviations, correlations, chi squares, t-tests, and analyses of variance, by use of alphabetical equipment, complete presentation of data can be accomplished in any prescribed fashion.

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BUDGET

DIVERSIFIED PROBLEMS DIVISION

July 1, 1947 - July 1, 1948

Code	Section	Personnel No.	Personnel Salaries	Materials & Supplies	Equipment	Total
3410	Fly Genetics	7	$ 16,000	$ 1,000	$ 1,000	$ 18,000
3420	Mouse Genetics	10	19,500	2,000	---	21,500
3430	Blood	7	18,520	5,000	2,500	27,000
3440	Surgery	14	39,900	7,750	7,200	54,850
3450	Immunity	3	4,500	1,800	1,200	7,500
3460	Protein Metabolism	5	12,700	5,000	7,300	25,000
3470	Theoretical Problems	2	5,000	2,500	2,500	10,000
3480	Histological Service	4	6,500	4,500	1,000	12,000
3490	Statistical Service	10	19,000	9,000	---	28,000
	TOTAL	61	$141,620	$39,530	$22,700	$203,850

1152030

C. SERVICE DIVISION:

Chief of Division: Fred A. Bryan, M.D., Instructor in Radiology and Medicine, The University of Rochester

1. INDUSTRIAL SERVICES (3301):

The services included in this section are radiological surveys, dust surveys, β and α counts on special materials supplied, γ and β determinations on plant workers by film badges, etc.

2. DERMATOGLYPHICS (3302):

This section is concerned with the reading and interpreting of fingerprint impressions (by Dr. Roger H. Harvey) for special materials plants and other Atomic Energy Commission installations.

3. SPECIAL FILM BADGE STUDY (3303):

A special study is to be performed to cover investigations of the effects of pressure, heat, and time of development after exposure and combinations of all three on the stability of the Type K film. It will also include a comparative study of films at Harshaw Chemical Company.

4. SPECIAL POWER STUDY (3304):

A special study is contemplated by Dr. Fred A. Bryan in conjunction with the Industrial X-ray Laboratory of The University of Rochester. It will concern itself with a study of possible power development from the heat generated by absorption of γ, β, and α radiations, in various metals.

5. MEDICAL CONSULTANT OFFICE (3310):

An Eastern Branch Office of Dr. Stafford L. Warren's office

1152031

(Medical Consultant to the Atomic Energy Commission) will be maintained at the Rochester Project. It will act in a district-wide consulting capacity to the various manufacturing concerns, and when necessary, to Operations CROSSROADS.

6. FIELD SERVICE CONTINGENCY FUND (3311):

The Medical Consultant Office feels it advisable to have a special section set up for the purpose of hiring special consultants from time to time such as those hired for the purpose of preparing the Japanese reports, etc.

1152032

BUDGET

SERVICE DIVISION

July 1, 1947 - July 1, 1948

Code	Section	Personnel No.	Personnel Salaries	Materials & Supplies	Equipment	Total
3301	Industrial Services	5½	$16,800	$18,700	$4,500	$40,000
3302	Dermateglyphics		2,500	1,500	—	4,000
3303	Special Film Badge Study		—	3,000	—	3,000
3304	Special Power Study		5,000	5,000	—	10,000
3310	Medical Consultant Office	1½	7,000	1,000	—	8,000
3311	Field Serv. Contingency Fund (Medical Consultant Office)	—	15,000	10,000	—	25,000
	TOTAL	7	$46,300	$39,200	$4,500	$90,000

1152033

D. RADIOLOGY AND BIOPHYSICS DIVISION:

Chief of Division: William F. Bale, Associate Professor of Radiology, The University of Rochester

1. RB-1: Studies of the Metabolism of Polonium in Experimental Animals -- Research up to the present time has outlined in a reasonably satisfactory manner the rate at which polonium is excreted in the white rat following oral, intravenous, and subcutaneous administration, as well as following absorption as a vaporized polonium dust breathed into the lungs. There remain several aspects of the metabolism of polonium deserving of further investigation because of the importance of this material to the work of the Atomic Energy Commission. The proposed studies under this major problem are as follows:

RB-1a: Long-Term Retention of Inhaled Polonium in Lungs of Rats and Other Animals -- To determine the rate at which polonium is removed from the lungs of workers who may be exposed to this material in dust or vapor form.

RB-1b: Studies on the Biochemical Nature of Polonium Metabolism -- To determine the chemical form or forms in which polonium exists in the body and to determine the biochemical factors influencing its distribution and excretion from the body.

RB-1c: Therapeutic Agents and Methods -- To determine whether or not BAL (British Anti-Lewisite) and related compounds influence the excretion of polonium from the body and its distribution in the body following intravenous or subcutaneous administration.

The following Sections of the Division are utilized on Problem RB-1: Instrumentation, Tracer Chemistry, and Radiation Physiology.

1152034

2. RB-2: Human Tracer Studies with Elements of Importance to the Medical Section -- To fulfill requests already made from the Medical Section, it is planned to carry out human tracer studies with the following radioactive elements as well as the animal studies and instrumentation necessarily preliminary to a competent carrying out of the program on human subjects. The purpose of these studies, for all the elements listed below except for radiolead, will be (a) to measure excretion as a function of the amount of the element in the body and of time after administration in order that a more exact relationship can be established between exposure and amounts stored and excreted, and (b) to pick up any deviations in metabolism between human subjects and experimental animals. In the case of radiolead, the data obtained will be useful in correlating the metabolism of the radioactive heavy metals listed below with that type of heavy metal poisoning for which the greatest clinical experience is available.

RB-2a: Polonium (continuation of present studies)

RB-2b: Plutonium (rechecks on present patients)

RB-2c: Uranium (probable continuation of studies now underway)

RB-2d: Thorium

RB-2e: Radiolead

RB-2f: Radium

The following Sections of the Division are utilized on Problem RB-2: Instrumentation, Tracer Chemistry, and Metabolism.

3. RB-3: Long-Term Chronic Exposure of Animals to Ingested Radioactive Materials -- Following accumulation in the body of long-lived

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radioactive elements of which substantial amounts are retained over periods of months or years, it is believed at the present time that the detrimental effects most likely to occur are due to chronic changes that will show up years after the initial exposure. Relatively short-term chronic experiments such as we have conducted with polonium, plutonium, and radium, extending over periods of a year in white rats, still make necessary extensive extrapolations in time and in animal size and life span to use this data to arrive at a tolerance or permitted dosage level for humans. We, therefore, propose to initiate experiments with these elements extending not only over the complete life span of white rats but also of dogs and other animals considerably closer to a human subject in size and life span. Obviously such experiments represent a program of several years' duration, but the importance of the anticipated results make it difficult to sidestep the necessity of carrying them out.

The following Sections of the Division are utilized on Problem RB-3: Radiation Physiology.

4. RB-4: Acute and Chronic Exposure of Experimental Animals to Radon and Thoron -- Adequate chronic exposures of experimental animals to radon and thoron have never been carried out. The urgency of doing this is well indicated. We, therefore, propose to set up exposure chambers for animals and to conduct acute and chronic exposures with associated physiological and pathological studies necessary to indicate an experimental tolerance value for radon and thoron in human subjects.

The following Sections of the Division are utilized on Problem RB-4: Instrumentation and Radiation Physiology.

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The following Sections of the Division are utilized on Problem RB-6: Instrumentation, Radiation Physiology, Radiation Chemistry, Spectroscopy, and Radiation Mechanics.

7. RB-7: Development of Improved Methods for Radium Determinations in Human Subjects -- Where large numbers of personnel are exposed to the possibility of radium ingestion, as occurs for example during the preliminary handling and first stages of processing of the ore from which uranium is to be extracted, it is very desirable to know at what rate tolerance concentrations are being approached by the personnel involved. One wishes to know, if possible, whether under a certain set of working conditions, certain personnel are accumulating radium so that tolerance values will be reached in a year or whether radium accumulation in terms of the tolerance amount is negligible. For it is possible that many workers will stay in this occupation many years, and it is not desirable to force them into a change of occupation because of radium accumulation in their bodies or to run the risk of endangering their health at a later time. The present method of measuring radium accumulation in the human body, by measurements of alpha activity in one liter samples of exhaled air, is entirely inadequate for this purpose. It seems quite evident that the best general method of approach is that of concentrating the radon from the dust samples much larger than one liter. It is proposed to continue a program of research in this field now underway in order that such a method will be developed to the point that it is suitable for routine use and gives results in which entire confidence can be placed.

The following Section of the Division is utilized on Problem RB-7: Instrumentation.

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8. RB-8: Analytical Procedures as a Contribution to Work Mainly Carried Out in Other Divisions of the Project.

RB-8a: Dust Particle Size Determination with the Electron Microscope -- It is proposed to utilize the electron microscope for particle size determination and exposure of experimental animals to uranium, thorium, and beryllium compounds and to use auxiliary electron defraction apparatus for the identification of dust particles.

RB-8b: Ultraviolet Spectroscopy -- Techniques utilizing ultraviolet spectroscopy will be applied to the analyses for uranium, beryllium, thorium, and such other elements as seems expedient and practical.

RB-8c: Radon Determinations -- It is planned to continue analyses of air samples from special materials plants for radon, and determinations of radium fixed in the bodies of employees of such plants by radon analyses of expired air.

The following Sections of the Division are utilized on Problem RB-8: Instrumentation, Spectroscopy, and Radiation Mechanics.

9. RB-9: Development of Procedures and Applications for Radioisotopes Produced in the Chain Reacting Pile -- It is proposed to carry out research in which radioactive elements will be used as tools in obtaining fundamental information of significance to medical science. It is also proposed to investigate the therapeutic usefulness of these materials particularly in the treatment of neoplastic disease.

RB-9a: Tracer Studies:

1. The development of organic synthetic methods for introducing isotopes into biologically important compounds.

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2. The development of routine methods for isolation of intermediary metabolites containing radioisotopes.

3. The development of methods for determining radioisotopes in biological materials.

4. The development of the methods applicable to biological and medical problems principally in the field of protein metabolism.

RB-6b: Development of Therapeutic Applications:

1. Thyroid neoplasms (I 131). (In collaboration with various divisions of Strong Memorial Hospital.

2. Other neoplasms (synthesis and testing of various radioactive compounds for preferential uptake in various tumors.

The following Sections of the Division are utilized on Problem RB-6: Instrumentation and Tracer Chemistry.

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BUDGET

RADIOLOGY AND BIOPHYSICS DIVISION

July 1, 1947 - July 1, 1948

Section	No.	Personnel Salaries	Materials & Supplies	Equipment	Total
Administration	10	$ 21,600	$ 2,000	---	$ 23,600
Instrumentation	15	48,400	5,000	$ 7,000	60,400
Tracer Chemistry	14	41,400	7,000	7,000	55,400
Radiation Physiology	18	48,700	9,500	4,200	62,400
Radiation Chemistry	7	19,300	2,000	2,700	24,000
Spectroscopy	7	23,000	2,000	2,000	27,000
Radiation Mechanics	4	15,000	3,000	5,000	23,000
Metabolism	9	15,600	1,000	600	17,200
TOTAL	84	$233,000	$31,500	$28,500	$293,000

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IV.

BUDGET

ADMINISTRATIVE DIVISION

July 1, 1947 - July 1, 1948

Code	Section	Personnel No.	Personnel Salaries	Materials & Supplies	Equipment	Total
3001	Administration	7	$ 28,000	$ 1,000	$ 500	$ 29,500
3003	Telephone	2	3,300	3,700		7,000
3004	Health	7	11,000	2,000		13,000
3005	Library	2	3,000	250		3,250
3006	Duplicating	2	2,400	2,000		4,400
3007	Security	15	30,000	50		30,050
3008	Shops	9	12,000	10,000	2,000	24,000
3011	Accounting	3	9,000	500	1,000	10,500
3012	Purchasing	1	2,400	50		2,450
3013	Supply Unit	5	13,000	3,000	1,000	17,000
3014	Maintenance	9	13,500	2,000	500	16,000
3015	Transportation	2	4,000	1,500		5,500
3017	Travel (Freight)			4,000		
	(Travel)			15,000		
3018	Rent, Utilities, & Insurance:					
	(Insurance)			15,000		
	(Rent)			10,000		
	(Gas & Electricity)			12,000		
3019	Overhead					
	TOTAL	64	$131,600		$5,000	$284,914

PRIVACY ACT MATERIAL REMOVED

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V.

OVERALL BUDGET

ROCHESTER PROJECT, ATOMIC ENERGY COMMISSION

July 1, 1947 - July 1, 1948

Code	Division	Personnel No.	Personnel Salaries	Materials & Supplies	Equipment	Total	Contingency	Overall Total
3000	Administration	64	$131,600	$148,314	$ 5,000	$ 284,914	$27,642	$ 312,556
3100	Radiology & Biophysics	84	233,000	31,500	28,500	293,000	7,000	300,000
3200	Pharmacology	96½	255,780	50,510	13,900	320,190	33,019	363,209
3300	Service	7	46,300	39,200	4,500	90,000	10,000	100,000
3400	Diversified Problems	61	141,620	30,530	23,700	203,850	20,386	183,466
	OVERALL TOTAL	312½	$818,300	$300,054	$74,600	$1,201,954	$98,046	$1,300,000

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VI.

PROPOSED EDUCATIONAL PROGRAM

It is our firm conviction that one of the most effective ways of rendering a service to the Atomic Energy Commission in general, and specifically in carrying out the local program, is for the Rochester Project to participate in an educational program. This program is being submitted not for actual approval at this time but for consideration by the Atomic Energy Commission in the formulation of their overall educational policies. It must be understood that we have not had the opportunity to discuss such a program with many educators in the University who would of necessity have to take part in such an endeavor. The thoughts which we wish to convey, therefore, merely reflect the ideas of the Rochester Project personnel only, and should not be construed as necessarily representing the ideas of the Administrative Offices of the University of Rochester.

The work participated in by the various categories of students listed on the following pages must be of an unclassified nature as the written theses required for advanced degrees must be available to the Graduate Council of the University for approval.

Before this program can be inaugurated, additional building facilities will have to be erected adjacent to the Medical School. The funds for this undertaking should be allocated by the Atomic Energy Commission rather than by the University per se as the program we are suggesting is a public responsibility rather than a private one.

Plan for Proposed Educational Program

The type of instruction that will be sought at Rochester may be divided into three main categories:

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1. Persons desiring short-term intensive instruction on specific research or health monitoring techniques.

2. Persons already holding M.D., Ph.D. degrees, or the equivalent, desiring a one-year course covering Industrial Toxicology, Radioactive Measurements in Tracer Techniques, and Health Physics.

3. Graduate students desiring to carry out full-time work in the University over a period of several years leading to Ph.D. degrees either in Industrial Toxicology and Pharmacology or in Biophysics.

The three categories of students listed above are discussed in greater detail below.

1. SHORT-TERM STUDENTS

It is likely that there will be a considerable demand in the future for short-term instruction leading to a mastery of certain individual research techniques that the student will carry back and apply in his home laboratory. The typical example of the field in which such instruction may be desired is that of certain radioactive isotopes preparatory and measurement techniques. As well as we can foresee, this probably also represents the field of instruction for which there will be the greatest demand.

Almost the only way for a student to obtain competent instruction in a short period is for him to work with and observe someone who is actually conducting research in which this technique is utilized.

Instruction in any one technique cannot be given efficiently to more than a small group at one time. These students therefore should presumably be rather evenly distributed over the year in order that apparatus and facilities be available, thus affording each student individual experience in their use.

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2. ONE-YEAR FELLOWSHIPS

A very important class of students seems likely to be mature scientists with M.D., Ph.D. degrees, or the equivalent, who desire instruction in essentially the whole field of Radiology, Health Physics, and Industrial Toxicology, in order that they may assume responsible roles in controlling health hazards in other locations concerned with the production or utilization of nuclear energy.

Three seminars, designed principally for orientation purposes, are given each week at the present time and partially cover the above fields of interest. They are as follows:

a. The Radiology and Biophysics Seminar -- Sponsored by the Rochester Project and available to selected Project personnel and Radiology Department (Strong Memorial Hospital) personnel.

b. The Pharmacology Seminar -- Sponsored by the Pharmacology Department of the Medical School and available to interested personnel of both the Rochester Project and the Pharmacology Department of the Medical School.

c. The Rochester Project Radiology and Biophysics Seminar -- Sponsored by the Radiology and Biophysics Division of the Rochester Project and available to interested Project personnel only.

In any comprehensive educational program these seminars are most useful but must be supplemented by intensive courses in which laboratory work is emphasized. The following three courses, therefore, are proposed to be given for this purpose, utilizing at each instance about one-half the time of the student.

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1. Industrial Toxicology -- This course, to be given by the Division of Pharmacology and Industrial Toxicology, will cover the toxic properties of metals and solvents, also hygiene, RPD, dust sampling, ventilation, dermatology, industrial first-aid, organ analyses, and forensic medicine. The course would involve laboratory periods, conferences, and lectures. It will occupy about one-half the time of the student for three months.

2. Radioactive Measurements and Tracer Techniques -- This course, to be given by the Division of Radiology and Biophysics, will offer comprehensive laboratory experience in the measurement of alpha, beta, and gamma activities, also instruction in elementary electronics, absolute calibration of instruments and standards, sample preparation, tracer techniques and isolation methods. It will involve laboratory instruction, conferences, and lectures, and will occupy about one-half the time of the student for a period of three months.

3. Health Physics -- This course, to be given either by the Division of Radiology and Biophysics or the Service Division, will supplement those courses previously described, covering the biological effects of radiations, measurement of radiation from the health standpoint and other techniques and theory pertinent to this subject. It will occupy about one-half the time of the student for a period of three months.

It is felt that these courses should not be given concurrently but at separate times so that the student will be able to take each in turn and still have time always available for other activities. They might play a part in an existing program as an assistant or co-worker. If they came to Rochester Project with a program of interest to the Atomic Energy Commission,

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facilities might be made available for them to conduct investigations with whatever assistance and consultations which our staff can afford.

In certain instances also, additional courses or work in the Medical School or College of Arts and Sciences may be indicated.

A certificate indicating competent tenure of this fellowship would be awarded at the end of the year.

3. GRADUATE STUDENTS

Our close connection with the University of Rochester Graduate School makes it possible and desirable to give full-time training over a period of several years to competent candidates leading to Ph.D. degrees in the fields of Biophysics or Pharmacology and Industrial Toxicology. Almost undoubtedly there will be a real demand for personnel with competent training in these fields.

Ph.D. Degree in Biophysics

A. Prerequisites: College major in physics, chemistry, or the biological sciences.

B. Course of Study: (Graduate School, The University of Rochester)

1. Chemistry 131-132: Advanced Organic Chemistry -- An advanced study of the reactions of carbon compounds and the theories of organic chemistry.

2. Mathematics 11-12: Analytical Geometry and Calculus -- A course presenting ideas indispensable for further mathematical study. This work is fundamental in the application of mathematics to physics.

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3. Physics 113: Modern Physics — A survey of the field of atomic physics with particular emphasis on recent trends. Introductory undergraduate courses in physics and mathematics prerequisite.

4. Physics 121-122: Electricity and Magnetism — Lectures and recitations on the theory of electrostatics, magnetostatics, and electrodynamics, including a detailed analysis of A.C. circuits and the elementary theory of electromagnetic waves.

B. Course of Study: (Medical School, The University of Rochester)

1. Biochemistry 1 — The course consists of a study of the chemical compounds and processes in the living animal body with special reference to man. The laboratory course is largely quantitative, covering the more important processes and methods for the examination of tissues and fluids.

2. Physiology A:— Nerve, Muscle, Central Nervous System, Circulation, Respiration, and Kidney — An introductory course for medical students dealing particularly with circulation, respiration, muscular activity, the nervous system, and special senses. Lectures, conferences, and laboratory work. Physiological principles treated in the lectures are illustrated in the student laboratory wherever possible by experiments on human subjects.

3. Physiology B: Nutrition and Endocrinology —

1152048

A Study of the physiology of digestion, absorption, secretion, energy metabolism, heat regulation, internal secretions, and vitamins.

Ph.D. Degree in Industrial Toxicology and Pharmacology

A. Prerequisites: College major in chemistry.

B. Course of Study: (Graduate School, The University of Rochester)

1. Chemistry 131-132: Advanced Organic Chemistry -- An advanced study of the reactions of carbon compounds and the theories of organic chemistry.

B. Course of Study: (Medical School, The University of Rochester)

1. Biochemistry 1 -- (as listed on Page 38)
2. Physiology A -- (as listed on Page 38)
3. Physiology B -- (as listed on Page 39-40)

and

4. Pharmacology 1: The study of the biochemistry, toxicology, and pharmacological actions of the more important drugs. Special clinical lectures emphasize the therapeutic applications. Laboratory exercises are planned to illustrate the effects of drugs on organ systems. A brief acquaintance with current practices in anesthesia is gained through the courtesy of the Department of Surgery.

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While personnel are available at the present time to teach certain of the courses listed under (1) Short-Term Courses, (2) One-Year Fellowships, and (3) Graduate Students, it is estimated that the majority of the proposed instruction could not be started before the latter part of 1947 or the early part of 1948 without gross neglect of our present activities and without sacrifice of other work.

Once the proposed educational program gets underway, it is estimated that the following number of students could be accommodated each year:

1. Intensive One-Month Course -- Possibly three or four students is a desirable number at any one time for this work. This means that in the course of one year, instruction may be given to 36-48 students.
2. Fellowships of One-Year Duration -- Ten to twenty students per year.
3. Graduate Students -- Twenty graduate students by the Pharmacology Division and ten graduate students by the Radiology and Biophysics Division plus ten graduate students working primarily in other divisions of the Project -- Total: Forty graduate students.

BUDGET

The University as a whole figures that the instruction of medical students or graduate students costs about $3,000 each above the services received from the students. Assuming a total of thirty graduate students on this basis, the figure is $90,000.

If one assumes ten fellowships of one year's duration costing $3,000 each, the total expended under this category will be $30,000.

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If intensive short-term training is given to an average of three students per month on this cost basis, the expenses involved will be $9,000.

So far, we have assumed no salaries will be paid to one fellowship holders. If salaries of $5,000 annually are paid with ten fellowships, the total expended will be $50,000.

One-Month Courses (36 students)	$ 9,000
One-Year Training (10 fellowships)	30,000
Graduate students (30 fellowships)	90,000
Sub-Total	$109,000
Salaries for one-year fellowships (10) @ $5,000 each	50,000
TOTAL ANNUAL BUDGET	$159,000

It is difficult at this time to supply more than roughly approximate budgetary figures, and therefore the above represents only a probable budget for a program of this type.

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