MLM - 69
THIS DOCUMENT CONSISTS OF 8 PAGES
THIS IS COPY 11 OF 208
Contract No. AT-33-1-GEN-53

BIOLOGICAL AND HEALTH RESEARCH PROGRAM FOR FISCAL YEAR - 1949

Submitted by
Monsanto Chemical Company
Central Research Department
Dayton, Ohio

Director	Dr. C. A. Hochwalt
Laboratory Director Units 3,4,&5	Dr. M. M. Haring
Health Division Director	Dr. J. L. Svirbely

Date: March 12, 1948

Distributed: MAR 15 1948

Author: J. L. Svirbely

SECRET

UNCLASSIFIED

DISTRIBUTION

1. - C. A. Hochwalt
2. - M. M. Haring
3. - J. L. Svirbely
4. - W. P. Jolley
5. - Area Manager
6. - Area Manager
7. - Area Manager
8. - Area Manager
9. - Area Manager
10. - Area Manager
11. - Area Manager
12. - Area Manager
13. - Area Manager
14. - Area Manager
15. - Area Manager
16. - Area Manager
17. - Central Files
18. - Central Files
19. - Central Files
20. - Central Files

UNCLASSIFIED

SECRET

1081815

The prime interest of the Dayton Area is the isolation, purification, and utilization of polonium; therefore, this area can best appreciate the problems encountered in handling large quantities of polonium and/or its derivatives. In addition to the ordinary problems encountered in laboratory operations (radiation and toxicological hazards), the morale of the personnel is an important factor to be considered. If biological research is done in this area, better morale should be maintained because the personnel will be cognizant of the efforts being made to protect them from the radiation and toxicological exposure effects. In the past our people have not been satisfied with tolerances based on other than indisputable experimental evidence. Such evidence is almost nil. Both chronic and acute toxicity studies must be thoroughly investigated. Only such long time studies can satisfactorily settle the question whether too much or too little emphasis is being placed on protection from radiation hazards. Finally, it is most inadvisable to risk possible cross-contamination with various other radioactive materials.

Biological research with polonium and/or its derivatives implies a study of the effects upon the living organism. The alteration of structure and function of the organism as a whole and/or of its component parts in the apparently normal animal must be studied as well as the responses of the body when concurrent infection is present.

A tentative list of experiments that are planned to be conducted during the 1949 fiscal year is given below:

A. Biological Group

1. Acute Toxicity Studies

These studies are important not only in observing the biological effects following large doses of various substances but in determining the level of dosage to be used for chronic exposure studies.

Occasionally, in our production unit, people are inadvertently exposed to high concentrations of polonium and polonium compounds. Very little clinical, hematological, pathological, distribution, and excretion data are available concerning effects of polonium on these people. It is hoped that some information may be obtained from such experiments not only to determine the biological half life of polonium in the body but also the threshold value in the kidney in order to determine the actual tolerance or maximum permissible concentrations to substitute for the calculated values currently used.

a. The LD_{50} (lethal dose killing 50 per cent of the animals in a fixed time) of polonium and polonium

compounds will be determined in mice and rats of definite age and in both sexes, by intravenous and parenteral administration.

b. The relative toxicity of polonium and polonium compounds in different vehicles will be compared by skin absorption in mice, rabbits, cats, and dogs.

c. Distribution of polonium in the different tissues, feces, and the body fluids at definite time intervals will be determined following administration by intravenous and parenteral administration as well as skin adsorption. Rats, guinea pigs, mice, rabbits, and dogs will be utilized in these experiments.

d. Autoradiographs will be made of sections of the kidneys, testicles, and ovaries at different time intervals following administration of large doses of polonium and polonium compounds.

e. Respiration studies of various tissues with polonium and polonium compounds are planned.

f. The effects of polonium on the reproduction system in rats and mice following intravenous and parenteral administration will be studied.

g. The effect of polonium on the oestrus cycle in rats will be determined by the exercising cage.

h. The effect of polonium on the liver and renal function tests in dogs will be determined.

i. Intubation studies will be made with polonium in rabbits and dogs to determine sites of the lung retention by autoradiographs. These studies are of importance since the lung retention of polonium may be the limiting factor in estimating the polonium tolerance values for humans.

2. Chronic Toxicity Studies With Polonium and Polonium Compounds

Although valuable information may be obtained from acute toxicity studies, the effects may not be similar to those obtained by smaller doses over a long period of time. Industry is more concerned with chronic experiments since people are exposed to small concentrations of toxic substances over long periods of time.

Chronic experiments will be initiated by intravenous injection and skin absorption in rats, mice, dogs, rabbits, and guinea pigs over a long period of time, with particular

reference to those species of animals considerably closer to the human subject in size and life span. Data obtained from these experiments may be used to arrive at a tolerance for maximum permissible concentrations for humans.

In these experiments the following items will be stressed:

a. Hematological studies in rats, rabbits, and dogs.

b. Urine metabolism and excretion of polonium in rats and dogs.

c. Autoradiographs of kidneys and reproductive organs in rats, rabbits, mice, and dogs.

d. Sterility experiments in rats, mice, and dogs.

e. The effect on the oestrus cycle in rats as determined by the exercising cage.

f. Liver and renal function tests in dogs.

g. Intubation studies in rabbits and dogs to determine sites of the lung retention by autoradiographs.

h. Tissue respiration studies.

3. Studies of the Possible Production of Mutants With Acute and Chronic Dosage Levels in Plant, Marine and Animal Life Including Molds and Fruit Flies

The results of these experiments may be limiting factors in establishing the maximum permissible concentration of polonium.

4. Acute and Chronic Studies of the Effect of Polonium in Bacterial Flora of Sewage Disposal Plants

Little information is available at the present time concerning the effect of radioactive substances, as such or in conjunction with other industrial wastes, on the modern biological sewage plants.

5. Acute and Chronic Studies in the Basal Metabolism, Blood Pressure, Cardiography, Blood and Plasma Volume Changes in Dogs

These experiments may yield information of diagnostic importance.

6. Study of Therapeutic Agents and Polonium Metabolism

a. The effect of therapeutic agents in the elimination of polonium from the body will be studied in acute and chronic exposures in dogs and rats. Data obtained from such a study may be used to increase the rate of elimination of polonium from humans, thus reducing the duration of exposure and the time lost by personnel from their jobs.

b. Studies of the biochemical factors involved in the distribution and excretion of polonium from the body will be initiated. At the present time, very little information is available as to which state polonium exists in the body. The methods used in colloid and steroid chemistry will be utilized in these experiments.

7. Biological Effects, Methods of Measurement and Protection Against Radiation from Special Neutron Sources Prepared at This Site

Permissible exposure levels for different tissues have to be established to adequately protect our personnel.

Some of the proposed experiments for acute and chronic exposures with various species of animals are:

a. Hematological studies.

b. Sterility experiments - effect on reproductive organs.

c. Oestrus cycles in rats.

d. LD_{50} (lethal dose killing 50 per cent in a fixed time).

8. Experiments With Beryllium

Inhalation studies with various species of animals on pure beryllium metal dust of various particle sizes will be made with reference to the lungs because of its special importance to this site.

The personnel requirements for the proposed research program should include:

1 Chief of Section (have 1)
2 Biochemists (have 1)
1 Pathologist (candidates being interviewed)
1 Physiologist (have 1)
1 Bacteriologist (candidate under consideration)

1 Geneticist (have 1)
1 Pharmacologist with training in toxicology (unfilled)
1 Plant Physiologist (eventually)
5 Biologists (have 4)
5 Chemists (have 2)
3 Laboratory Aides (unfilled)
1 Electron-microscopist (unfilled)
1 Hematologist (have 1)
1 Statistician (have 1)

B. Special Problems Group

1. Low Activity Research

Along with other miscellaneous problems, research will be centered toward the evaluation and developing improvements in determining the quantity of polonium present in samples of urine, feces, blood, mud, and river water. These procedures are necessary to establish the background of our product in the surrounding area, routine survey and personnel monitoring.

The personnel to do the work should consist of:

4 Chemists (have 4 - Two now on loan to the Production Group)
1 Research Chemist (unfilled)

2. Survey and Decontamination Group

Research will be directed toward studies on the decontamination and precaution of contamination in equipment, instruments, floors, clothing, etc. Improvements in the decontamination procedures are necessary to meet A.E.C. regulations.

The personnel to do the work should consist of:

1 Research Chemist (unfilled)
1 Chemist (have 1)
1 Laboratory Aide (have 1)

C. Health Instrument Group

The Health and Development Group of the Health Instrument Section functions solely for the Health Division.

It is planned to center the research work in the following items:

a. Parallel plate alpha counting equipment.
b. Continuous fast neutron monitoring equipment.

SECRET

c. Portable fast neutron equipment.
d. Fast neutron monitoring film efficiency.
e. Low count counting rate meters.
f. Air sampling equipment.
g. Efficiency of air filters used to filter exhaust air from plant.
h. Scintillation counting.
i. Instrumentation of biological research group.
j. Two geometry alpha counters for plated samples which at the present time have a counting geometry.

The personnel to do this work consists of:

2 Senior Electronics Engineers (have 2)
3 Junior Electronics Engineers (have 3)
1 Junior Draftsman (have 1)
1 Senior Research Physicist (unfilled)

SUMMARY

By doing the work at the Dayton Area, better coordination of the actual problems encountered with the biological research work can be maintained.

A tentative program for biological and medical research by Monsanto Chemical Company at the Mound Laboratory has been submitted.

The estimated budget for this work for the fiscal year July 1948 to July 1949 is as follows:

Salaries	$225,000.00
Supplies	160,000.00
Miscellaneous	115,000.00
Total	$500,000.00

It should be noted that the extent and amount of research work done in the temporary quarters in the Warehouse and at Unit 5 depends on several factors. In addition to getting the personnel and training them, considerable time will be spent setting up the laboratories in the Biological Building as well as in the other buildings at Unit 5.

Approved by M. M. Haring
M. M. Haring

cm

SECRET