APPENDIX A

AGENDA FOR MEDICAL COMMITTEE FOR ATOMIC RESEARCH

JANUARY 23, 24, 1947

I. Review and approval of past program. (Medical summary 1943-46 to be reviewed and approved if possible).

II. Scope of Research Program 1946-47. (Appendix A)

(University of Chicago) Argonne National Laboratories
University of Rochester
University of California
Hamilton
Stone
Columbia University
University of Washington, Seattle
Monsanto Chemical Corp. (Clinton Laboratories) USPHS
Monsanto Chemical Corporation (Dayton)
Los Alamos Western Reserve University

Contracts Awaiting Approval:

University of Virginia
University of Tennessee

III. Recommendations for Future Research Policy

A. Scope of fundamental work (that approved in September meeting) (Appendix A)
B. Human Testing with special materials

IV. Organization of Medical Responsibilities

A. Advisory Committees

1. Advisory Committee on Medical Research and application (Tolerances, Standards and Hazard Interpretations in addition to research programs).
2. Advisory Committee on Industrial Medicine and Toxicology.
3. Advisory Committee on Health Physics.

B. Recommendation for the continuation of operation of the Medical Division at the present level with the available reduced force now in that office as well as salary schedule.

C. Training Program

1. Statement of the urgent need for qualified trained physicians.
2. Source of physicians.
   A.S.T.P.
   Civilian
3. Recommendations for specific training program.

V. Recommendations for Medical Director and Delineation of Responsibilities.

VI. Representation on Advisory Board to Atomic Energy Commission

VII. Release of Information

Recommendation for a mass meeting of all present and former Atomic Energy Commission medical researchers, at which time a program (4 days) would present accurate information on all medical aspects related to atomic energy then available for security clearance. This meeting would be open to scientific personnel in all parts of the country. The following suggestions are pertinent:

A. Approximately 6-8 months preparation would be required.
B. A central location should be selected to insure a maximum attendance.
C. Abstracts of the program should be circulated at least one month prior to the date of the meeting (similar to that procedure used by the Federated Societies of Physiology, Biochemistry, etc.) These abstracts should be approved by a previously selected editorial board before release.
D. Consideration should be given toward the founding of a new scientific society whose major interest would be based on problems of radiobiology as related to medical interest. The Journal of Radiobiology now being launched could well be made the official journal of this society.

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Types of study include I General Studies in Radiation including (1) physical measurement of radiation, (2) biological effects of radiation (3) methods of detection of minimal radiation damages and (4) methods for the prevention of radiation injuries. II Hazards due to special Materials (for non-radioactive, radioactive and fission materials) (1) degree of toxicity (2) preventative measures. III Special Production Hazards and IV Hazards of Military Uses.

Argonne National Laboratories (University of Chicago)

1. General physiological picture of acute and chronic radiation.
2. Radiation effect on blood clotting, lymphocyte distribution and spread of infection.
3. Toxic effects of external radiation and absorbed radioactivity.
4. Response of blood cells to various types of radiation.
5. Chronic effects of radiation and radioactive materials in animals.
6. Mode of action of radiation in carcinogenesis.
7. Chemical and physiological basis of radiation effects.
8. Metabolism of radioactive elements.
9. Instrument standardization, design, etc.

University of Rochester

Radiation and Radiology Section

1. Instrument design, measurement standardization, industrial monitoring.
2. Biological effect of tracer amounts of polonium, radium and uranium in human and animal subjects. Application of tracer experiments to serve other parts of the project.
3. Physiological effects of exposure to acute and chronic radiations including radio isotopes; search for therapeutic methods of value.
4. Development of possible chemical technique or methods of detection of radiation damage and the mechanism by which such effects are produced.
5. By means of spectroscopic methods to study distribution of uranium and other heavy metals of importance in animal tissue; search for possible clues as to the method of bony deposition of radioactive materials.
6. Study of the time intensity factor in radiation and development of methods of producing instantaneous exposure to radiation (A bomb effect).
7. Study of the metabolism of plutonium, polonium, radium, etc., in human subjects.

Pharmacology

1. Study of the inhalation toxicity of various uranium, beryllium and thorium compounds. Studies in the mechanism of production of inhalation toxicity.

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2. By chemical technique, studies of the mechanism of uranium fixation in bones, uranium complex function, methods of excretion of uranium.
3. Toxicity of uranium, beryllium and thorium compounds by ingestion.
4. Pathological effects of uranium, beryllium and thorium poisoning and mechanism by which produced.
5. Physiological effects of uranium, beryllium and thorium poisoning.

Experimental Surgery

1. Clinical, hematological and pathological effects of acute lethal radiation.
2. Methods of bone marrow transplantation.
3. Studies in bone marrow reserve and radiation effect.
4. Tissue culture studies related to bone marrow production.
5. Effect of folic acid and rutin on marrow regeneration.
6. Studies in metabolism of iodine by thyroid (15%).

Experimental Hematology.

1. Comparative study of blood histamine and hematological effects in cells.
2. Studies on life cycle of blood platelets.
3. Studies on life cycle of WBC leukocytes.
4. Studies on marrow reserves after radiation.
5. Evaluation of coagulation defects following irradiation.
6. Techniques for early detection of hematological changes resulting from ionizing radiation.

Genetics

1. Continuation of studies of effect of chronic radiation on mice.
2. Continuation of studies on effect of acute and chronic radiation (X-ray) on Drosophilia.
3. Histogenetics.

University of California

1. Studies of the metabolism of plutonium, uranium and fission products in rats and man.
2. Fission product tracer studies.
3. Metabolism of radium, actinium, americium and curium in animals and man.
4. Studies (pilot) on possibly hazardous artificially induced radioactive elements, i.e. chromium, nickel, etc.
5. Beryllium tracer studies.
6. Treatment of plutonium poisoning.

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7. Behavior of fission products in soils.
8. Biological effects of fission recoils.
9. Search for other U compounds which will localize in organs other than liver and spleen (15%).
10. Biological effect of disintegration products of boron and lithium of the neutron irradiation (15%).
11. Study of element 85 in the thyroid (15%).
12. Training of Crossroads personnel.
13. Studies in whole body radiation of human subjects.
14. Studies on metabolism of radioactive iodine in animals and man.

Columbia University

1. Studies on the measurement of fast neutrons for biological dosage.
2. Development of a method of measuring neutron dose by chemical means.
3. Measurement of radioactive isotopes for biological and medical application.
4. Correlation of tissue doses and biological effects produced by external irradiation and by radioactive isotopes internally administered.
5. Exploratory biological experiments to extend use of radio-active isotopes as tracers on therapeutic agents (15%).
6. Studies of the fundamental biological action of ionizing radiation.
7. Measurement of the radiation of radioactive isotopes to provide data for the protection of personnel and films in transit.

University of Washington (Seattle)

1. Acute and chronic effects of external radiation on fishes.
2. Breeding studies on salmon following radiation.
3. Studies on the effects of Hanford effluent on salmon and trout.
4. Effect of internally deposited radioactive materials on fishes.
5. Field studies on the effect of possible Hanford pollution on fish life of the Columbia River.
6. Plankton experiments - effect of radiation on higher forms (new).
7. Feeding experiment on deposited radioactive materials (new).

Monsanto Chemical Corp. (Clinton Laboratories) USPHS

1. Continuation of studies on the biological effect of slow fast and thermal neutrons on rats and mice.
2. Continuation on studies on the comparative biological effect of penetrating radiation.
3. The effect of internally deposited plutonium on bone healing.
4. Cytological program on the biological effect of radiation on simple cells and tissue.
5. Instrumentation and techniques of radiation monitoring.

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Monsanto Chemical Co. (Dayton) New program being organized.

1. Biological effects following chronic exposure of animals to polonium by inhalation and parenteral administration.
2. Correlation between chronic exposure of workers and polonium excretion rate.
3. Mechanism of action of polonium toxicity.
4. Development of special health physics technique for specific use in polonium purification.

Los Alamos

1. Fundamental studies on the effect of acute radiation exposure.
2. Treatment of acute radiation disease.
3. Methods of detecting early radiation changes.
4. Metabolism of plutonium, U^{235} and other radioactive materials.
5. Detection of accumulated plutonium in the lungs.
6. Biochemical studies of nucleoproteins and the effect of radiation on the fundamental physiology of the cell.
7. Detailed study of absorption of plutonium from contaminated wounds.
8. Any special problems arising from medical hazards peculiar to this project.

Western Reserve University

1. Investigation of the toxic effects of thorium and its isotopes.
2. Comparative studies on the biological effect of external radiation and that from internally deposited radioactive materials.
3. Use of radioactive isotopes in fundamental biological research.

These general titles are given inasmuch as a program has not been actively formulated.

Contracts Awaiting Approval:

University of Virginia - Dr. Alfred Chanutin

Study of the effects of various types of radiation (alpha, beta, gamma & neutrons) on the circulating blood proteins by electrophoresis and protein fractionization technique. To determine whether means of early detection of radiation damage can be accomplished in this way.

University of Tennessee - Dr. Henry Wills

Study of the mechanism of toxic effects of uranium and other heavy metal compounds on the kidney. This is a continuation of Dr. Wills' work with the Rochester Manhattan Project during the war and contributes to that general study.

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University of California, Los Angeles - Dr. Stafford L. Warren

1. The mechanism of blood vessel injury by radiation.
2. Bone marrow injury by radiation, its repair and treatment.
3. Mechanism of "metal" deposition in bone and mechanism of removal from bone.
4. Protein degradation following radiation and chemical injury.

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I General Studies of Radiation

The radiations encountered in nuclear fission as well as those encountered from naturally radioactive substances divide themselves into the following types: Alpha rays, beta rays, gamma rays and neutrons. Information available from the literature on previous studies indicates a rather extensive knowledge of the biological effects of X-rays and gamma rays and very little information on alpha and beta rays and neutrons.

The programs were and are organized using the following basic outline:

A. The Physical Measurement of Radiation of various types - Here it is necessary to develop methods of accurately measuring and standardizing the dosage of radiation to be used in the biological experimentation and measurement of the extent of any hazardous radiation which might be found in a plant area.

B. The Biologic Effects of Radiation. Because of the known deleterious effect of radiation on the animal organism, it becomes necessary to determine the effect of controlled dosages of the various types of radiation on various animal species, so that such observations can be used in the control of possible human exposure.

The types of biological effect possible to study are:

(1) The Survival Time or percentage that the effect of a given dose will reduce the normal life span of different animal species.

(2) The Genetic Effects of radiation as manifested in the development of abnormal individual types from changes in the hereditary mechanism.

(3) Histopathological Changes as demonstrated by abnormal changes in the make-up of the various body tissues.

(4) Physiological Changes produced by the alteration of the normal functioning of animal tissues following radiation.

(5) Biochemical and Enzymatic disturbances which are the potential source of these physiological abnormalities.

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C. Methods for the Detection of Minimal Radiation Damage are developed directly from observation of the above types and are applied to study of the human individual or worker. These include studies on:

(1) Biochemical and Enzymatic Changes which may be detected and which, if measurable, can be corrected before irreversible damage has taken place. Examples of such change would be effects on the metabolism of coproporphyrins, excretion of abnormal substances in the urine and the like.

(2) It has been known that radiation depresses the function of the hematopoetic system and detailed study is indicated to detect early changes under controlled dose radiation with all blood elements under continuous observation.

(3) The Production of Anatomical Changes such as epilation, skin erythema, and alterations in the integrity of the skin and the like must likewise be studied under controlled dosage.

D. Studies are likewise indicated on methods for the prevention of radiation injuries. These include:

(1) Methods of physical detection of external radiation by the development of sensitive direct reading instruments capable of the detection of amounts of radiation well below those necessary for demonstrable injury to the animal subjects.

(2) Methods for the determination of harmful amounts of radioactive dusts and gases in air, in water and the like. Many radioactive materials like radium are deposited in the body and in such locations produce injury to tissue. Methods based on the determination of dangerous amounts of these substances by examination of the excreta and direct measurements of the body itself are necessary.

E. Protective Measures. Studies on the efficiency of shielding against radioactive materials, the efficiency of exhaust and ventilating systems against dangerous amounts of dusts, the development of protective clothing and devices, and the development of remote control processing methods have been extremely important in the Manhattan District protection program to date and will continue into the future.

F. The possible therapeusis of radiation damage by the use of replacement therapy for the damaged bodily elements, as well as the reduction in the exposure following deposition of radioactive materials in the body deserves considerable study. Replacement of the damaged hematopoetic elements destroyed by severe radiation exposure offers one possibility; detection and neutralization of unknown toxic substances produced by radiation and other such difficult problems deserve consistent and detailed study.

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All the above studies are necessary on alpha, beta and gamma rays and neutrons of varying intensity. In addition, the radiation from the radioactive substances to be discussed has likewise to be considered. Also, the effects of acute and chronic exposure must be determined because of their dissimilarity.

II Hazards Due to Special Materials

For brevity it is preferable to discuss the potential toxicity of special materials by first indicating the type of study to be carried out, followed by the presentation of these materials on which studies have been necessary.

A. First, an actual determination of the toxicity of a substance must be made indicating how poisonous it may be in both acute and chronic exposure. In this way the toxic levels may be avoided in laboratory and plant environments.

(1) The mode of entrance into the body by ingestion, inhalation and skin absorption must be studied as different manifestations and degrees of toxicity may be produced by each route employed.

(2) A careful analysis must be made as to the character of the biological changes with the production of physiological, histopathological and biochemical evidences of damage incurred.

(3) The nature of these injuries and the mechanism by which they occur must likewise be studied inasmuch as this affords information as to the necessary protection and indicated therapy after exposure.

B. Preventative measures require study.

(1) The effectiveness of physical methods for the removal of hazardous dusts, reduction in skin contact and prevention of ingestion must be measured, and methods for accurate determination of such hazards must be developed and used. The use of certain chemicals, ointments, and the like as protective measures must be studied as to their efficiency.

(2) Protective devices such as respirators and clothing must be tested on required substances against which they will be used.

(3) Finally, appropriate investigation of therapeutic measures to be used in the treatment of both acute and chronic poisoning states should they occur in industrial exposure must be made.

Completion of all phases of the above program on a variety of substances provides complete information as to the medical aspects necessary to be considered in protection of the worker, prevention of injury and treatment of injury should it occur.

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C. Substances on which studies of this type are necessary are:

(1) Uranium and its compounds

a. Uranium metal and its chemical compounds, oxide, nitrate, chloride, bromide, totra and hexa-fluorids, sodium and ammonium sulfates.

b. Uranium chain of heavy metals

Uranium X1
Uranium X2
Radium
Polonium

c. Fission products of cleavage of U-235 and plutonium.

d. Artificial isotopes of uranium - 232, 234, etc.

(2) Thorium and its chain

(3) Plutonium

(4) Special Accessory Materials

a. Fluorocarbons
b. Fluorine
c. Beryllium
d. Others

III Production Hazards

The results of studies made on the materials discussed above are applied for the prevention and control of industrial hazards arising in the large manufacturing areas where these materials are used in large amounts.

A. In the Electromagnetic and Diffusion Methods for the isolation of uranium 235 the major hazards are from the uranium compounds, the concentration of uranium X1 and X2, and the special accessory materials and by-products formed in the process of manufacture.

B. In the graphite pile where plutonium (239) is produced on a large scale, the hazards are from the alpha, beta and gamma rays, neutrons, the plutonium metal and its compounds, the various radioactive fission products resulting from the pile operation.

C. The chemical isolation of polonium following its formation in the pile incorporates hazards from alpha radiation following absorption into the body.

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D. Study of the medical aspects of plant programs aside from the determination of the effect of radiation and chemical toxicity, include additional information obtained from plant investigations as from:

(1) Clinical survey of all exposed personnel.

(2) Monitoring of hazards by special instruments and methods.

(3) Surveys of new types of graphite piles and production equipment.

IV Hazards of Atomic Catastrophe in Production Areas.

A. Immediate Effects

(1) Radiation - the radiation occurring at the time of the explosion coupled with blast and heat causes biological effects which may differ from those occurring following other acute known effects from gamma and neutron radiation, and demand study.

(2) Blast - the blast of atomic explosion is so intense and may have totally different types of shock waves, recoil waves with other unique biological effects which should be investigated.

(3) Heat - The intense burns from actinic type of radiation have not been studied. This also includes the combination effect of all three items in this group: blast, radiation and heat.

(B) Delayed Effects

(1) Protective Devices - study of methods of protection against the radioactivity deposited at the time of blast.

(2) Decontamination - methods of decontamination of soil and the like must be worked out for cleaning up active areas.

(3) Investigative Equipment - special equipment must be developed and tested for use in investigating bombed areas.

(4) Study of casualty effects - field study of fission clouds, possible injury to water supply, soil and the like, human damage by population surveys.

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(5) Study of treatment of all immediate effects such as radiation, heat and blast.

(6) Preparation of pertinent information in proper form for use by catastrophe units in production areas.