MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : Consultants

DATE: November 26, 1979

FROM : Dr. Charles U. Lowe, M.D.
Special Assistant to the Director

SUBJECT: Meeting on November 29, 1979

We are happy that you will be able to join us on November 29 for the purpose of helping to draft an important element of what will become a Federal Strategy for Research into the Biological Effects of Ionizing Radiation. On November 7, a large group of consultants convened at NIH for this purpose; however, it was realized that one or several important areas had been overlooked or were not adequately represented among the initial group of consultants. The meeting on November 29 is scheduled to help rectify this deficiency. The group that will convene will address the research needs relating to the biological effects of radiation in space, specifically those from high Z radiation.

To give you a better appreciation of what the overall effort entails, we are enclosing a copy of the letter mailed to the consultants who met with us on November 7. The accompanying material from our meeting contractor, CSR, Incorporated, is of course pertinent to your convening at NIH on November 29.

Enclosures

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

October 26, 1979

Dear:

The Secretary, HEW, is required by law (P.L. 95-622 as amplified by supporting statements in the Congressional Record, October 14, 1978) to develop a comprehensive strategy for research into the biological effects of ionizing radiation supported or conducted by the Federal government. This strategy must reflect not only the needs of agencies with mandates to develop new knowledge, but also that research required by regulatory agencies to meet their responsibilities for protecting the public health. The Secretary has delegated this responsibility to Dr. Donald S. Fredrickson, Director of the National Institutes of Health.

This demanding and challenging responsibility requires the involvement of all Agencies and Departments having relevant programs. Accordingly, the Secretary chartered a committee chaired by Dr. Fredrickson, to act as a focal point in discharging this obligation. The Committee on Federal Research Into the Biological Effects of Ionizing Radiation has membership drawn from twelve Departments and Agencies, and has begun the process of formulating the Federal strategy.

While the Congressional intent was to limit the strategy to Federally funded or conducted programs, the Committee realized early in its deliberations that the success of the undertaking would depend in large part on its ability to recruit the advice and assistance of a large number of scientists pursuing their research in institutions of higher learning, private and public laboratories, and in private sector industry. Accordingly, a schedule of activities evolved to permit an interplay between these scientists and Federal officials.

On November 7 we plan to convene a selected group of scientists to consult on the drafting of an outline of research strategy that will be further developed by the Committee. The consultants have beeen chosen because they have an incisive grasp of a well defined area of research and, in many instances, a broad and comprehensive understanding of research issues as they intersect with public policy, consumer concerns, and political realities.

A preliminary and abbreviated outline of research has been developed by the Committee and contains twelve primary elements forming fairly well defined disciplinary clusters. The outline may provide no more than a starting point for discussion and need not be accepted in either form or substance. Approximately six consultants will be asked as a group to review a single element of this outline for organization, completeness, relevance, scientific opportunity, and the need for research supported by public funds. By the end of the day, we would expect to receive from each group of consultants a relatively detailed compilation of the research agenda they would recommend for Federal support.

From each group of consultants we expect to seek authors for what we have chosen to call "Scientific Projection Papers." These documents may be prepared by single authors or developed collaboratively. Some groups might choose to suggest the name of a scientist who may not have participated in the meeting on November 7 to write the "Projection Paper." The number of "Scientific Projection Papers" needed will vary among the disciplinary areas. We would expect advice on the requisite number.

The "Scientific Projection Papers," oriented toward disciplines, must have as a primary goal a justification for inclusion of the subject matter in a Federal research portfolio. They should be neither a "state of the art" summary nor a compendium of relevant science. Rather, we would expect a carefully reasoned document, placing the particular element of research into perspective, identifying the needs and opportunities, defining scientific questions to be answered, and the relation of this aspect of research to the larger total. At present, we cannot be precise about length, but we do not expect to receive voluminous documents. Ten to twenty typescript pages should suffice.

A limited number of papers of another sort will also be sought. These will be "issue papers" traversing a number of disciplines encompassing not only science related to the biological effects of ionizing radiation, but also the interplay between this body of knowledge and the need for and development of public policy. In addition, they should articulate, whenever appropriate, those problems which research alone cannot solve and must rely on the political process for resolution. This group of "issue papers" will serve to frame the scientific process, delineating both its strengths and limitations, and indicate how research can illuminate and guide the formulation of public policy. It seems particularly important to address matters which are of immediate concern to the public. The Committee will have selected the topics for "issue papers" in advance of November 7, but consultants may feel free to add additional titles.

All papers must be completed by February 1, 1980. These will be collated, printed, and be made available to the scientific community and to the public after February 20.

On March 10-11, we will convene an open meeting at which time the overall strategy will be discussed publicly. Authors of papers will be asked to present a synopsis of their recommendations, and the audience (Committee members, consumers, public interest groups, public administrators and scientists) will have an opportunity to comment, challenge or bless.

The product of this meeting should provide the essential material needed by the Committee on Federal Research Into the Biological Effects of Ionizing Radiation to fashion a well-groomed "Draft Federal Strategy." This "Draft" will be forwarded to a committee of the National Academy of Sciences for review on or before May 1, 1980. The Academy has a sitting committee reviewing current Federal research into the biological effects of ionizing radiation and will thus be uniquely prepared to provide a critique of the "Draft Federal Strategy." Within two months, the Academy Committee will return the "Draft" with comments, at which time the Committee will consider further recommended changes and modifications. It will be submitted in final form to the Secretary, Department of Health, Education, and Welfare for transmittal to the Congress by December 31, 1980.

This letter carries with it an expression of appreciation from the Committee and its chairman Dr. Donald S. Fredrickson. We are pleased that you have agreed to consult on this very demanding responsibility.

Should you have any questions, please feel free to contact me (301-496-3283) or my associates whose telephone numbers are noted at the bottom of this letter.

Sincerely,

Charles U. Lowe

Charles U. Lowe, M.D.
Special Assistant to
the Director

Dr. Oddvar F. Nygaard
Special Assistant to the Director
National Cancer Institute
301-496-9326

Dr. Elliott H. Stonehill
Research Planning Officer
National Cancer Institute
301-496-9326

CSR, Incorporated
Suite 500
805 15th Street, N.W.
Washington, D.C. 20005

Dr. Sherman Vinograd
Medical Director
St. Mary's Hospital
707 South Mills Street
Madison, Wisconsin 53715

CSR

Federal Strategy for Research into the Biological
Effects of Ionizing Radiation

High Z Radiation

November 29, 1979

National Institutes of Health
Building 31, Room 5A-16
Bethesda, Maryland

Participant List

Dr. Charles M. Barnes
Johnson Space Center
Mail Code SD-5
Houston, Texas 77058
(713) 483-5281

Dr. George W. Casarett
Professor of Radiation Biology
and Biophysics, and of Radiology
University of Rochester Medical Center
601 Elmwood Avenue
Rochester, New York 14642
(716) 275-3893

Dr. Stanley B. Curtis
Senior Staff Biophysicist
Lawrence Berkeley Laboratory
Building 74, Room 159B
#1 Cyclotron Road
Berkeley, California 94720
(415) 486-6389

Col. John Pickering, Ret.
Aerospace Medicine
Brooks Airforce Base
San Antonio, Texas 78235
(512) 536-3414

Dr. Paul Rambaut
Manager, Biomedical Research Program
NASA - Headquarters
SBR-3
400 Maryland Avenue, S.W.
Washington, D.C. 20546
(202) 755-3723

Dr. Charles Sondhaus
Associate Professor of Radiological
Sciences
University of California at Irvine
College of Medicine
Irvine, California 92717
(714) 634-5607

Dr. Epaminonda W. Stassinopoulos
Astrophysicist
NASA - Goddard Space Flight
Center
Code 601
Greenbelt, Maryland 20771
(301) 344-8067

Dr. Sherman Vinograd
Medical Director
St. Mary's Hospital
707 South Mills Street
Madison, Wisconsin 53715
(608) 251-6100 x398

Dr. Robert W. Wood
Director, Pollutant
Characterization and Safety
Research Division, EV-34
Office of Health and Environment
Research
U.S. Department of Energy
Mail Code E-201
Washington, D.C. 20045
(301) 353-3213

FUNCTIONAL OUTLINE OF RESEARCH STRATEGY

A. Sources and Pathways of Exposure

1. Background Radiation

    a. Geographic differences
    b. Time trends in exposure
    c. Space radiation (solar, cosmic)

2. Medical Exposures

    a. Diagnostic Exposures

        1) Radiographic procedures
        2) Radioisotope procedures
        3) Benefit/risk considerations

    b. Radiotherapy

        1) Radiation quality
        2) Synergism with other modalities
        3) Tissue injury and sequelae

3. Occupational Exposures

4. Releases to Environment

    a. Sources (including radioactive wastes and accidental releases)
    b. Physical transport - air, water, soil
    c. Biological transport - plants, animals, food
    d. Human transport to target tissue - uptake, metabolism, fate

5. Exposure in the Home

B. Reduction of Exposure

1. Occupational Radiation Protection (including shielding)

2. Improvement of Medical Techniques

    a. Dose optimization - treatment planning
    b. Amelioration techniques
    c. Quality assurance of radiological diagnosis
    d. Reduction of non-essential doses
    e. Source development and controls

3. Amelioration of radiation effects from accidental exposures

C. Improvements in Radiation Measurement and Dosimetry

1. Measurement methods and instrumentation
2. Measurement and prediction of dose distribution
3. Dosimetry of internal emitters

D. Fundamentals of radiation interactions with matter

1. Physics of radiation interactions
2. Chemistry of radiation interactions
3. Microdosimetry - track structure and radiobiological models

E. Dose-Effect Relationships

1. Epidemiology

a. Pre-disease measures
b. Extrapolation models
c. Competing risks
d. Suitability of study populations
e. Theoretical biological models

2. Somatic Effects-Carcinogenesis

a. Tissue and cell sensitivity, inducibility, incidence
b. Time course of events
c. Projection models of future disease risk
d. EFESTH
e. Cofactors, host factors
f. Dose rate, radiation quality
g. Dose response models

3. Non-Cancer Somatic Effects

a. Early (fertility, implantation, pregnancy)
b. Embryo (fetus, teratogenesis)
c. Organ-specific effects (normal and cancerous tissue)
d E2 (a-g) apply also to E3

4. Genetic Effects (Hereditary)

    a. Chromosome breakage
    b. Gene mutation-extrapolation from experimental systems to humans
    c. Cumulative effects
    d. Long range effects

        1) Background genetic disease
        2) Sensitive populations
        3) Rate of discount for future disease

5. Radiation Cell Biology

    a. Molecular effects (including DNA)
    b. Cellular end effects (Damage and repair processes, normal and tumor cells)

        1) Cell killing
        2) Mutagenesis
        3) Transformation
        4) Developmental processes

    c. Interactions with viruses and chemicals
    d. Genetic determinants
    e. Theoretical biological models

6. Chemistry

    a. Radiation chemistry - pulse radiolysis
    b. Chemical characterization of radiation damage to biological molecules
    c. Chemical repair
    d. Radiation modifiers (sensitizers - protective agents)
    e. Free radicals and electron transport in biological systems

THE FEDERAL STRATEGY FOR RESEARCH INTO THE
BIOLOGICAL EFFECTS OF IONIZING RADIATION

National Institutes of Health
November 7, 1979

LIST OF CONSULTANTS IN ORDER OF ASSIGNED CLUSTER

A - DIAGNOSTIC PROCEDURES

S. James Adelstein
Professor of Radiology
Harvard Medical School
25 Shatuck Street
Boston, Massachusetts 02115
(617) 732-1535

Reynold F. Brown
Director
Radiological Health Scientist
Education Project
University of California Medical Center
San Francisco, California 94134
(415) 666-4292

Roger J. Cloutier
Director
Radiopharmaceutic Internal
Dosimetry Center
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830
(615) 576-3437

Peter Joseph
Assistant Professor of Clinical
Radiology
Department of Radiology
Columbia University College
of Physicians and Surgeons
Columbia Presbyterian Hosptal
New York, New York 10032
(212) 694-3158

Elliott Lasser
Professor of Radiology/Acting Vice Chancelor
of Health Science
University of California
San Diego School of Medicine
La Jolla, California 92093
(714) 294-6604

B - TECHNOLOGY DEVELOPMENT

Bengt E. Bjarngard
Director
Division of Physics and Engineering
Radiation Therapy Department
Harvard Medical School
444 Binney Street
Boston, Massachusetts 02115
(617) 732-3596

Harold Fischer
Professor and Chairman
Department of Radiology
University of Rochester
Rochester, New York 14642
(716) 275-2733

Earle C. Gregg
Professor of Radiology - Physics
Department of Radiology
Case Western Reserve University
Cleveland, Ohio 44106
(216) 444-3522

Robert Loevinger
Center for Radiation Research
National Bureau of Standards
National Physics Building
Room C - 210
Washington, D.C. 202345
(301) 921-2364

John Rundo
Senior Biophysicist
Argonne National Laboratory
9700 South Cass Avenue
Argonne, Illinois 60439
(312) 972-4168

Roger Schneider
Director
Division of Electronic Products
Bureau of Radiological Health
Food and Drug Administration
500 Fishers Lane
Rockville, Maryland 20854
(301) 443-6536

Warren K. Sinclair
Associate Laboratory Director
Argonnne National Laboratory
Building 202
Argonne, Illinois 60439
(312) 972-3804

Edward W. Webster
Professor of Radiology
Harvard Medical School at
  Massachusetts General Hospital
Department of Radiology
Fruit Street
Boston, Massachusetts 02114
(617) 726-3078

C - THERAPY

Gould A. Andrews
Professor of Medicine and Radiology
University of Maryland Medical School
Baltimore, Maryland 21201
(301) 528-6890

Malcolm A. Bagshaw
Professor and Chairman, Department of
  Radiology
Director of Radiation Therapy Division
Stanford Univeristy School of Medicine
Stanford, California 94305
(415) 497-5650

J. Martin Brown
Associate Professor
Division of Radiobiology Research
Department of Radiology
Stanford Medical Center
Stanford, California 94305
(415) 497-5115

Juliana Denekamp
Cancer Research Center
Gray Laboratory
Mt. Vernon Hospital, Northwood
Middlesex, HA6 2RN
England

Stanley B. Field
MRC Cyclotron Unit
Hammersmith Hospital
Ducane Road, London W12 OHS
England

David H. Hussey
Department of Radiotherapy
Professor of Radiotherapy
M.D. Anderson Hosptial
 and Tumor Institute
6723 Bertner Street
Houston, Texas 77030
(713) 792-3400

C - THERAPY (Cont'd.)

Clarence C. Lushbaugh
Chairman
Medical and Health Sciences Division
Oak Ridge Associated Universitites
P.O. Box 117
Oak Ridge, Tennessee 37830
(615) 576-3090

Robert G. Parker
Professor and Chairman
Department of Radiation Oncology
University of California at Los Angeles
Center for the Health Science
Los Angeles, California 90024
(213) 825-9304

Lawrence N. Rothenberg
Assocate Attending Physicist
Department of Medical Physics
Memorial Sloan - Kettering Cancer Center
1275 York Avenue
New York, New York 10021
(212) 794-7722

Glenn Sheline
Vice Chairman
Department of Radiology
University of California Medical Center
San Francisco, California 94143
(415) 666-4815

J. Robert Stewart
Professor and Head of Division of
Radiation Oncology
Department of Radiation Therapy
Medical Center
University of Utah
Salt Lake City, Utah 84132
(801) 581-8793

John M. Yuhas
Associate Director
Cancer Research and Treatment Center
900 Camino del Salud N.E.
University of New Mexico
Albuquerque, New Mexico 87131
(505) 277-5938

D - PATHWAYS TO MAN

Lynn Anspaugh
Section Leader for Analysis
and Assessment
Environmental Sciences Division
Lawrence Livermore Laboratory
P. O. Box 5507
Livermore, California 94550
(415) 422-3880

Bruce Boecker
Inhalation Toxicology
Research Institute
P. O. Box 5890
Albuquerque, New Mexico 87115
(505) 264-6565

Steven A. Book
Associate Research Physicist
University of California at Davis
Laboratory for Energy Related
Health Research
Davis, California 95616
(916) 752-1339

Richard F. Foster
7 Stag Lane
P. O. Box 4263
Sunriver, Oregon 97701
(503) 593-1934

John H. Harley
Director
Environmental Measurements
Laboratory
Health and Safety Laboratory
Department of Energy
376 Hudson Street
New York, New York 10014
(212) 620-3616

Burton E. Vaughn
Manager
Ecological Department
Battelle Memorial Institute
Pacific Northwest Laboratories
P. O. Box 999
Richland, Washington 99352
(509) 942-3602

E - ECOSYSTEMS AND ENVIRONMENT

Stanley I. Auerbach
Director of Environmental
Sciences Division
Oak Ridge National Laboratory
P. O. Box X
Oak Ridge, Tennessee 37830
(615) 483-5139

Merril Eisenbud
Professor of Environmental Medicine
Environmental Health Sciences
New York University Medical Center
Box 817
Tuxedo, New York 10987
(914) 351-2368

Philip Gustafson
Director
Division of Environmental
Impact Studies
Argonne National Laboratory
9700 South Cass Avenue
Argonne, Illinois 60439
(312) 972-3115

Charles Osterberg
Marine Scientist
Department of Energy
Mail, Stop E201
Germantown, Maryland 20545
(301) 353-3035

Vincent Schultz
Department of Zoology
Washington State University
Pullman, Washington 99164
(509) 335-3027

F - PHYSICS

John A. Auxier
Director
Industrial Safety
and Applied Health Physics
Oak Ridge National Laboratory
P. O. Box X
Oak Ridge, Tennessee 37830
(615) 576-5454

F - PHYSICS Cont'd.)

Randall S. Caswell
Chief
Nuclear Radiation Division
Center for Radiation Research
National Bureau of Standards
Room B109
Washington, D. C. 20234
(301) 921-2551

Mitio Inokuti
Senior Physicist
Argonne National Laboratory
Building 203
9700 South Cass Avenue
Argonne, Illinois 60439
(312) 972-4186

William C. Roesh
Staff Scientist
Battele - Pacific Northwest Laboratories
1646 Butternut
Richland, Washington 99352
(509) 942-3369

Lewis V. Spencer
Acting Chief of Radiation
Physics Division
Building 220, Room B-206
National Bureau of Standards
Washington, D.C. 20234
(202) 921-3201

Cornelius A. Tobias
Faculty Senior Scientist
Donner Laboratories
Building 10, Room 202
University of California
at Berkeley
Berkeley, California 94720
(415) 486-6173

James E. Turner
Physicist
Oak Ridge National Laboratory
P. O. Box X
Oak Ridge, Tennessee 37830
(615) 576-5454

G - CHEMISTRY

John G. Burr
Professor
University of Oklahoma
Department of Chemistry
Norman, Oklahoma 73019
(405) 325-4781

Aloke Chatterjee
Senior Scientist
Lawrence Berkeley Laboratory
University of California at Berkeley
Building 29, Room 216
Berkeley, California 94720
(415) 486-5415

Clive L. Greenstock
Research Associate
Medical Biophysics Branch
Atomic Energy of Canada, Limited
Meidcal Physics Branch
Whiteshell Nuclear Research Establishment
Pinawa, Canada ROE ILO
(204) 753-2311 Ext. 524

E. L. Powers
Professor of Zoology
Director of the Laboratory of
Radiation Biology and the
Center for Fast Kinetic Research
Radiation Biology Laboratory
University of Texas
131 Patterson Building
Austin, Texas 78712
(512) 471-4615

Peter Riesz
Research Chemist
National Cancer Institute
Building 10, Room B1-B50
Bethesda, Maryland 20205
(301) 496-4036

Michael G. Simic
Research Chemist
Food Enginering Laboratory
U.S. Army
NARADCOM
Natick, Massachusetts 01760
(617) 653-1000, Ext. 2221 or 2772

H - MOLECULAR EFFECTS INTERACTIONS WITH CHEMICALS AND VIRUSES

Bruce Castro
Research Director
for Health Effect
Northrop Services, Incorporated
P. O. Box 12313
Research Triangle Park, North Carolina 27709
(919) 549-0611 Ext. 228

Rufus S. Day
Research Cancer Institute
National Institutes of Health
Building 37, Room 3C-25
Bethesda, Maryland 20205
(301) 496-1470

Philip C. Hanawalt
Professor of Biology and Dermatology
Department of Biological Sciences
Heurim Laboratory
Stanford University
Stanford, California 94305
(415) 497-2424

Robert B. Painter
Laboratory of Radiobiology
University of California
at San Francisco
San Francisco, Calfiornia 94143
(415) 666-3154

Malcolm C. Paterson
Associate Research Officer
Radiation Biology Branch
Health Science Division
Chalk River Nuclear Laboratory
Chalk River, Ontario
Canada KOH 1JO
(613) 584-3311

James D. Regan
Senior Investigator
Biology Division
Oak Ridge National Laboratory
P. O.Box Y
Oak Ridge, Tennessee 37830
(615) 574-0800

H - MOLECULAR EFFECTS INTERACTIONS WITH CHEMICALS AND VIRUSES (Cont'd.)

Leonard J. Tolmach
Professor of Radiation
Biology/Anatomy
Department of Anatomy
Washington University
School of Medicine
660 South Euclid Avenue
St. Louis, Missouri 63110
(314) 454-3341

Susan S. Wallace
Professor of Microbiology
Department of Microbiology
New York Medical College
Valhalla, New York 10595
(914) 347-5836

I - MUTAGENESIS, TRANSFORMATION, CELL-KILLING

Earle J. Ainsworth
Manager
Bevalve Radiobiology -
Radiotherapy Project
Donner Laboratories
University of California
at Berkeley
Berkeley, Calfornia 94720
(415) 376-5748

Ernest H. Y. Chu
Professor of Human Genetics
Department of Human Genetics
University of Michigan Medical School
1137 East Catherine Street
Ann Arbor, Michigan 48109
(313) 734-1353

William C. Dewey
Professor of Radiation Biology
Department of Radiation Biology
Colorado State University
Fort Collins, Colorado 80523
(303) 491-5096

Mortimer M. Elkind
Senior Biophysicist
Division of Biomedical Research
Argonne National Laboratory
9700 South Cass Avenue
Argonne, Illinois 60439
(312) 972-3939

I - MUTAGENESIS, TRANSFORMATION, CELL-KILLING (Cont'd.)

Eric J. Hall
Professor of Radiology
Associate Director
Radiological Research Laboratory
630 West 168th Street
Columbia University College
of Physicians and Surgeons
New York, New York 10032
(212) 694-3551

Abraham W. Hsie
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, Tennessee 37830
(615) 574-1250

John B. Little
Professor of Radiobiology
Harvard University School
of Public Health
665 Huntington Avenue
Boston, Massachusetts 02115
(617) 732-1184

Raymond W. Tennant
Senior Staff Scientist
Biology Division
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, Tennessee 37830
(615) 574-0823

Paul Todd
Professor
Department of Cell Biology,
Biochemistry and Biophysics
403 Althouse Laboratory
University Park, Pennsylvania 16801
(814) 865-0242

J - SOMATIC EFFECTS I - CANCER

Roy E. Albert
Professor and Deputy Director
New York University Medical Center
Institute of Environmental Medicine
550 First Avenue
New York, New York 10016
(212) 679-3200

J - SOMATIC EFFECTS I - CANCER (Cont'd.)

Gilbert W. Beebe
Clinical Epidemiology Branch
National Cancer Institute
National Institutes of Health
Landow Building, Room A-521
Bethesda, Maryland 20205
(301) 496-5067

Frederick J. Burns
Profesor of Environmental Medicine
Institute of Environmental Medicine
New York University Medical School
Room 213
550 First Avenue
New York, New York 10016
(914) 351-5638

Kelly H. Clifton
Professor of Human Oncology and Radiology
Department of Human Oncology
and Radiation
University of Wisconsin Medical School
Clinical Sciences Center
600 Highland Avenue
Madison, Wisconsin 53706
(608) 262-1376

David G. Cogan
Chief, Neuro-Ophthalmology Branch
National Eye Institute
National Institutes of Health
Building 10, Room 13-S-259
Bethesda, Maryland 20205
(301) 496-1244

Marvin Goldman
Director
Laboratory for Energy-Related
Health Research
University of California
Davis, California 95616
(916) 752-1341

Frank E. Lundin
Chief, Epidemiologic Studies Branch
Division of Biological Effects
Bureau of Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852
(301) 443-4203

J - SOMATIC EFFECTS - I CANCER (Cont'd.)

Robert W. Miller
Chief, Clinical Epidemiology Branch
National Cancer Institute
National Institutes of Health
Landow Building, Room 5A-21
Bethesda, Maryland 20205
(301) 496-5785

Leonard M. Schuman
Professor and Director of Division
of Epidemiology
School of Public Health
University of Minnesota
Minneapolis, Minnesota 55419
(612) 373-8029

Roy C. Thompson
Senior Research Scientist
Biology Division
Battelle - Pacific Northwest Laboratories
331 Building, 300 Area
Richland, Washington 99352
(509) 942-3043

Robert L. Ullrich
Head of the Radiology Course
Biology Division
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, Tennessee 37830
(615) 574-0676

McDonald E. Wrenn
Professor of Pharmacology
and Director of Radiobiology Division
University of Utah College of Medicine
Building 522 - Radiobiology Division
Salt Lake City, Utah 84112
(801) 581-5917

K - SOMATIC EFFECTS II - NON-CANCER

Victor P. Bond
Associate Director
Brookhaven National Laboratory
Upton, Long Island, New York 11973
(516) 345-3332

Kenneth R. Brizzee
Head of Neurobiology
Delta Regional Primate Research Center
Tulane University
Covington, Louisiana 70433
(504) 892-2040

K - SOMATIC EFFECTS II - NON-CANCER (Cont'd.)

Eric W. Hahn
Associate Member
Sloan-Kettering Institute
410 East 68th Street
New York, New York 10021
(212) 794-7517

Eugene F. Oakberg
Senior Research Staff Member
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, Tennessee 37830
(615) 576-0865

Harvey M. Patt
Professor of Radiobiology and Physiology
Laboratory of Radiobiology
University of California at San Francisco
San Francisco, California 94143
(415) 666-1636

Kedar N. Prasad
Associate Professor
Department of Radiology
University of Colorado
School of Medicine
4200 East 9th Avenue
Denver, Colorado 86262
(303) 394-7830

Liane R. Russell
Section Head
Mutagenesis Teratogenesis
Biology Division
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, Tennessee 37830
(615) 574-0860

L - GENETICS

William F. Brandom
Professor of Biological Sciences
Department of Biological Sciences
University of Denver
Denver, Colorado 80210
(303) 753-2882

L - GENETICS (Cont'd.)

J. Grant Brewen
Director of Genetic Toxicology
Allied Chemical Corporation
Morristown, New Jersey 07960
(201) 483-1475

James F. Crow
Laboratory of Genetics
University of Wisconsin
506 Genetics Building
445 Henry Mall
Madison, Wisconsin 53706
(608) 263-1993

Frederick J. De Serres
Associate Director for Genetics
P. O. Box 12233
Research Triangle Park, North Carolina 27709
(919) 541-3492

Douglas Grahn
Director
Division of Biological and
Medical Research
Argonne National Laboratory
Building 202
9700 South Cass Avenue
Argonne, Illinois 60439
(312) 972-3819

James V. Neel
Chairman
Department of Human Genetics
University of Michigan Medical School
1137 East Catherine Street
Ann Arbor, Michigan 48109
(313) 764-5490

R. Julian Preston
Senior Research Staff Member
Biology Division
Oak Ridge National Laboratory
Oak Ridge, Tennessee 37830
(615) 574-1238

William L. Russell
Consultant, Biology Division
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, Tennessee 37830
(615) 574-0858

L - GENETICS (Cont'd.)

Paul B. Selby
Biology Division
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, Tennessee 37830
(615) 574-0855

M - EPIDEMIOLOGY

John B. Boice
Epidemiologist
Environmental Epidemiology Branch
National Cancer Institute
Landow Building, Room 3C-07
Bethesda, Maryland 20205
(301) 496-1691

Louis H. Hempelman, Jr.
Professor Emeritus of Experimental
Radiology
University of Rochester School
of Medicine
Rochester, New York 14642
(505) 455-2913

Seymour Jablon
Director of Medical Follow-up Agency
National Academy of Sciences
2101 Constitution Avenue, N.W.
Washington, D.C. 20418
(202) 389-6467

Joseph L. Lyon
Assistant Professor of Epidemiology
University of Utah College of
Medicine
50 North Medical Drive
Salt Lake City, Utah 84132
(801) 581-5270

Genevieve Mantanoski
Professor of Epidemiology
Johns Hopkins School of Hygiene and
Public Health
Room 2405
615 North Wolfe Street
Baltimore, Maryland 21205
(301) 955-3483

Louis Massé
Institute Lyon Bernard
Rennes, France
995-9236

Edward P. Radford
Professor of Environmental Epidemiology
University of Pittsburgh
Graduate School of Public Health
517 Tarron Hall
Pittsburgh, Pennsylvania 15261
(412) 624-3009

Joseph E. Rall
Director, Intramural Research Program
National Institute of Arthritis, Metabolism
and Digestive Diseases
Building 10, Room 9N-222
Bethesda, Maryland 20205
(301) 496-4128

Marvin A. Schneiderman
Associate Director for Science Policy
National Cancer Institute
National Institute of Health
Building 31, Room 10A-06
Bethesda, Maryland 20205
(301) 496-1611

John R. Totter
Institute for Energy Analysis
Oak Ridge Associated
Universities, Incorporated
P. O. Box 117
Oak Ridge, Tennessee 37830
(615) 576-3173

Warren Winkelstein, Jr.
Dean and Professor of Epidemiology
University of California at Berkeley
School of Public Health
19 Warren Hall
Berkeley, California 94720
(415) 642-4304

Meeting to Develop
the Federal Strategy for Research into the
Biological Effects of Ionizing Radiation

National Institutes of Health
November 29, 1979

High-Z Radiation Cluster

Tentative Outline of
Subjects to be Discussed

Environmental Physics

Definition of space radiation
Sources (types and fluctuation) high, low
Standard environment
Dosimetry (standard procedures, instrumentation)

Biological Effects of High-Z Particles

RBE (Q_f) of heavy particles
Microdosimetry
Special protection guides for workers (cyclotron, space)
Radiotherapy with high-Z particles

Operational Countermeasures

a) Radioprotective chemicals
   Partial-body shielding
   Post-exposure therapy (amelioration)
   Work/rest cycle

b) Warning measures
   Evasive actions

THE FEDERAL STRATEGY FOR RESEARCH INTO THE
BIOLOGICAL EFFECTS OF IONIZING RADIATION

November 7, 1979
National Institutes of Health

ALPHABETICAL CONSULTANT LIST

KEY TO CODING:

Letter		Disciplinary Cluster	Room Number
A	=	Diagnostic Procedures	6
B	=	Technology Development	6
C	=	Therapy	6
D	=	Pathways to Man	7
E	=	Ecosystems and Environment	7
F	=	Physics	8
G	=	Chemistry	8
H	=	Molecular Effects, Interactions with Chemicals and Viruses	9
I	=	Mutagenesis, transformation, Cell-Killing	9
J	=	Somatic Effects I - Cancer	10
K	=	Somatic Effects II - Non-Cancer	10
L	=	Genetics	10
M	=	Epidemiology	10

[A] S. James Adelstein
[I] Earle J. Ainsworth
[J] Roy E. Albert
[C] Gould A. Andrews
[D] Lynn Anspaugh
[E] Stanley I. Auerbach
[F] John A. Auxier

[C] Malcolm A. Bagshaw
[J] Gilbert W. Beebe
[B] Bengt E. Bjarngard
[D] Bruce Boecker
[M] John B. Boice
[K] Victor P. Bond
[D] Steven A. Book
[L] William F. Brandom
[L] J. Grant Brewen
[K] Kenneth R. Brizzee
[C] J. Martin Brown
[A] Reynold F. Brown
[J] Frederick J. Burns
[G] John G. Burr

[H] Bruce Castro
[F] Randall S. Caswell
[G] Aloke Chatterjee
[I] Ernest H.Y. Chu
[J] Kelly H. Clifton
[A] Roger J. Cloutier
[J] David G. Cogan
[L] James F.Crow

[H] Rufus S. Day
[C] Juliana Denekamp
[L] Frederick J. De Serres
[I] William C. Dewey

[E] Merril Eisenbud
[I] Mortimer M. Elkind

[C] Stanley B. Field
[B] Harold Fischer
[D] Richard F. Foster

KEY TO CODING (CONT'D)

[J] Marvin Goldman
[L] Douglas Grahn
[G] Clive L. Greenstock
[B] Earle C. Gregg
[E] Philip Gustafson

[K] Eric W. Hahn
[I] Eric J. Hall
[H] Philip C. Hanawalt
[D] John H. Harley
[M] Louis H. Hempelman, Jr.
[I] Abraham W. Hsie
[C] David H. Hussey

[F] Mitio Inokuti

[M] Seymour Jablon
[A] Peter Joseph

[A] Elliott Lasser
[I] John B. Little
[B] Robert Loevinger
[J] Frank E. Lundin
[C] Clarence C. Lushbaugh
[M] Joseph L. Lyon

[M] Louis Masse
[M] Genevieve Matanoski
[J] Robert W. Miller

[L] James V. Neel

[K] Eugene F. Oakberg
[E] Charles Osterberg

[H] Robert B. Painter
[C] Robert G. Parker
[H] Malcolm C. Paterson
[K] Harvey M. Patt
[G] E.L. Powers
[K] Kedar N. Prasad
[L] R. Julian Preston

[M] Edward P. Radford
[M] Joseph E. Rall
[H] James D. Regan
[G] Peter Riesz
[F] William C. Roesch
[C] Lawrence N. Rothenberg
[B] John Rundo
[K] Liane B. Russell
[L] William L. Russell

[B] Roger Schneider
[M] Marvin A. Schneiderman
[E] Vincent Schultz
[J] Leonard M. Schuman
[L] Paul B. Selby
[C] Glenn Sheline
[G] Michael G. Simic
[B] Warren K. Sinclair
[F] Lewis V. Spencer
[C] J. Robert Stewart

[I] Raymond W. Tennant
[J] Roy C. Thompson
[F] Cornelius A. Tobias
[I] Paul Todd
[H] Leonard J. Tolmach
[M] John R. Totter
[F] James E. Turner

[J] Robert L. Ullrich

[D] Burton E. Vaughn

[H] Susan S. Wallace
[B] Edward W. Webster
[M] Warren Winkelstein, Jr.
[J] McDonald E. Wrenn

[C] John M. Yuhas

AGENDA

COMMITTEE ON FEDERAL RESEARCH
INTO THE BIOLOGICAL EFFECTS OF IONIZING RADIATION

Federal Strategy For Research
Convening of Expert Consultants

HIGH Z RADIATION

November 29, 1979

National Institutes of Health
Building 31, Room 5A16
Bethesda, Maryland

8:30 a.m. Meeting Strategy

Dr. Charles U. Lowe
Special Assistant to the Director
National Institutes of Health

Comments

Dr. Oddvar F. Nygaard
Special Assistant to the Director
National Cancer Institute

9:00 a.m. Discussion of Issues

The group will be responsible for choosing a chairman.

COFFEE AVAILABLE IN CONFERENCE AREA

11:30 - 1:30 p.m. CAFETERIA OPEN FOR LUNCH

5:00 p.m. Adjournment

Before adjourning, the group must have prepared their recommendations for research, identified an author(s) for a "science projection paper" and if time permits address the list of cross cutting questions.

C. Barnes
S. Dominguez

Radiation Biology Research (HZE Particles)

General

HiZ particles is a relatively unexplored class of radiation and numerous basic studies must be done to determine its characteristics and General biological effectiveness. (low level, hi level, specific organ, etc)

Due to the size and complexity of accelerators required to produce HZE particles and the current lack of such facilities it will be necessary for activation of more accelerators to fulfill the requirement for research. This may require additional support facilities as well.

A. Animal Experimentation

2. Aloft

General

Due to the expense of operating ground based, monotype radiation sources it may be less expensive to operate in-Space research laboratories where multi-directional, multi energetic sources are available-free.

Research Required: Cost Benefit Analysis of Space VS Ground Experiments.

In lieu of the See Reverse

1. Prototype dedicated ~~Life Science~~ Bio-Radiation Experiment Satellite (In conjunction with other Life Sciences studies)

Research Required

Design + Develop spacecraft + support requirements

2. Fully dedicated Bio-radiation satellite

Research Required

Design + develop spacecraft + operational strategy

Develop capability for radiation-biology studies in space. (Spacecraft, support facilities

VINCENT & BARNES (1)

II RADIATION BIOLOGY

A- ANIMAL

2- ALOFT

a. DOSE-RESPONSE STUDIES

(1) VARIABLES

~~= EARLY, LATE, LIFE SHORTENING EFFECTS~~
~~= SPECIFIC ORGAN VS. WHOLE BODY EFFECTS~~
~~- LOW, INTERMEDIATE & HIGH DOSE~~
~~LOW LET HIGH LET~~

~~SPECIFIC ORGAN EFFECTS~~

- EARLY, LATE, LIFE SHORTENING EFFECTS
- SPECIFIC ORGAN, WHOLE BODY EFFECTS
- ~~CELL~~ TISSUE, CELL, BIOCHEMICAL +/OR GENETIC MATERIAL EFFECTS
- TYPE OF RADIATION TO WHICH EXPOSED
  - LOW LET ; HIGH LET
- DOSE, LOW, INTERMEDIATE, HIGH
- SINGLE VS. FRACTIONATED EXPOSURE

(2) ESTABLISH 2 OR 3 STANDARD EXPERIMENTAL ANIMALS (DOWN TO THE SUBSPECIES LEVEL) BY GROUND BASED STUDIES. SIMILARLY, SELECT & ESTABLISH A STANDARD TISSUE CULTURE AND CELL SPECIMENS.

(3) DEVELOPMENT AND SELECTION OF STANDARD BATTERY OF ~~DOSE~~ FLIGHT DOSIMETRY AND PLACEMENT (GROUND BASED STUDIES)

(4) DEVELOPMENT AND SELECTION OF A MINIMAL STANDARD SET OF RESPONSE DETERMINATION END POINTS TO BE EXAMINED. SENSITIVE BEHAVIORAL, EYE, etc, TESTS NEED TO BE DEVELOPED.

(5) DEVELOPMENT & SELECTION OF ACCEPTABLE BIOCHEMICAL AND GENETIC EVALUATION METHODS.

(6) DEVELOPMENT OF ACCEPTABLE FLIGHT SIMULATION TECHNIQUES FOR POST-FLIGHT ~~IMPLEMENTATION~~ OF PARALLEL CONTROL STUDIES.

(7) USE OF FLIGHT DATA TO DETERMINE POSSIBLE ~~SYNERGISTIC EFFECTS OF~~ DIFFERENT TYPES OF RADIATION TO WHICH ~~EXPOSED~~ — ~~BY APPROPRIATE POST-FLIGHT STUDIES~~ USING SIMILAR SPECIES.

(8) DETERMINE EFFECTS OF DOSE FRACTIONATION BY FLYING SAME ANIMALS (OR OTHER SPECIMENS) ON REPEAT FLIGHTS

(9) CROSS CORRELATE ANIMAL & HUMAN RESPONSES AS POSSIBLE ON A CONTINUING BASIS.

4. COMBINED EFFECTS

(1) FLIGHT STUDIES OF ANIMAL RESPONSES TO WELL-DEFINED AMBIENT RADIATION IN COMBINATION WITH 3 OR 5 LEVELS OF g (ZERO PLUS 2 LEVELS OF ARTIFICIAL g).

c. MECHANISMS OF RADIATION EFFECTS (BEST STUDIED ON THE GROUND)

II RADIATION BIOLOGY

B. HUMAN

1. GROUND BASED

a. GATHER ALL ~~RELIABLE~~ RETROSPECTIVE AND PROSPECTIVE DOSE-RESPONSE DATA FROM ALL RELIABLE SOURCES (THERAPY, ACCIDENTS). RE HTE, OBTAIN DATA FROM NCE SUBJECTS ON A CONTINUING BASIS. CAREFUL DOSIMETRY AND FOLLOW-UP EXAMINATIONS REQUIRED

b. ESTABLISH DOSE-RESPONSE DATA CORRELATION FACILITY, COMPUTERIZED, CONTINUING, & PROBABLY CENTRAL.

- INFORMATION COMMUNICATION TIES MUST BE EFFICIENT FOR QUICK RESPONSE

2. ALOFT

a. No ACTIVE HUMAN RADIATION EXPERIMENTS

b. ESTABLISH A CAREFULLY SELECTED MINIMAL BATTERY OF HISTORY, PHYSICAL AND LABORATORY EXAMINATION CRITERIA FOR IMMEDIATE AND LONG RANGE FOLLOW-UP OF ALL FLIGHT PERSONNEL FOR RETROSPECTIVE DOSE-RESPONSE ANALYSIS. THIS IS HEAVILY DEPENDENT ON A STANDARD ~~DOSIMETRY~~ AND WELL-SELECTED DOSIMETRY SET PROPERLY LOCATED ALOFT.

- THIS ALSO REQUIRES A DETAILED REPORT OF THE INDIVIDUAL'S PHYSIOLOGICAL RESPONSES

TO FLIGHT OR FLIGHTS PLUS FLIGHT INCIDENT & ENVIRONMENTAL DATA + TO RULE OUT OTHER POSSIBLE TECHNICAL INFLUENCES.

B. Human Studies Aloft Human radiation exposures will result from astronaut activities and ~~human's~~ will not be approved solely for purposes of ~~specifically to~~ studying particular biological effects.

Prior to flite - Physical Exams, based on potential lesions will be conducted

Post flite: immediate examination

follow up " for several years (life)

Research Needed ① Technique development as to how ~~to~~ space radiation effects in man resulting from can be measured ... small doses, large doses

② Technique development for determining relative radiation susceptibility between different human beings.

③ To determine Radiation Exposure limits for man in space - assuming a very brief, 1-5 year career.

④ Statistical comparison of male VS female response in HZE therapeutic response and in flite exposures.

Animal Ground studies

⑤ Comparative teratogenic effects in animals simulating man in various trimesters of Pregnancy.

⑥ Develop statistical cumulative data on relative effectiveness of HZE's at various ages.

IV Coordination

General

It is necessary that all radiation data produced within the government be coordinated. This might best be accomplished by establishing a "radiation effects data center" in which experimental results are tabulated, computerized and circulated to interested persons.

In conjunction with the above and specifically for HZE particle effects in-flight (aloft) the Russian government has collected numerous hours of experimental data from their space laboratories. This has not generally been made available (translated) for U.S. investigators. Translations should be a part of the data center.

Russians have been hesitant to attend outside meetings to present their data. The US government should host such efforts or assist international scientific organizations in sponsorship.

No research Required - Funding for meetings appropriate.

Rowland + Ward

Operational Countermeasures.

Body shielding

Ground based

- Application of current ~~cod~~ transport codes to evaluate various shielding configurations for variety of space radiation spectra and particle makeup
- Development of improved transport codes
- Development of organ shielding techniques
- Research into optimal designs for shelters
- Evaluation of prototype shielding concepts at accelerators that simulate space radiation

Aloft.

- Evaluation of prototype shielding concepts in flight

Radioprotectants

Ground Based

- State of Art review of radioprotectant literature with respect to high Z ions, particularly USSR data
- Expanded research to identify additional agents
- Research on effectiveness of combination therapy ie multiple drugs, nutritional concerns, other
- Basic research on structure-function relationships
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Aloft

- Drug distribution and utilization in the body at zero-gravity
- In flight evaluation of radioprotectant performance if suitable end point can be defined

Amelioration

- Research into chemicals which when taken post radiation may modify effects.
- Influence of physical countermeasures on radiation effect.

Stanley Curtis
E. J. Stassinopoulos

I

A. Definition of Environment

1. ~~Definition of Primary Environment: the following areas:~~

a. Energetic Particles

1. A requirement exists for a predictive technique which relates some solar or geophysical parameter (such as solar wind speed or D_{st}) to acceleration of electrons to high energies in the outer magnetosphere. The required output is: a) Spatial Distribution, b) Energy Spectra, and c) Flux Intensities.

2. Given an input distribution (spatial, energy spectrum, flux intensity) of energetic electrons in the outer magnetosphere, a model is needed which will detail the evolution of the distribution.

3. Manned applications require a short term prediction of magnetic storms and substorms. Particle acceleration and plasma injection are both major concerns.

4. A 'Disturbance Model' for prediction of flux enhancements due to solar or magnetospheric activity is required. It should have two forms: a typical storm, and a macro storm.

5. A requirement for synoptic measurements of solar wind parameters to predict intermediate term (30-60 days) averages of fluxes at synchronous altitudes exists.

6. A model which calculates the hardening of electron energy spectra in response to rapid diffusion caused by field-line loading is desired.

7. Current methods take several days to calculate the environment and dose for a new orbit. This must be shortened.

8. The long lead time (typically several years minimum) to get new data into a data base for modeling purposes must be shortened.

b. Solar Flare Protons AND Cosmic Rays

1. A predictive technique must be developed which will warn of anomalously large events (e.g., August 1972) hours or days in advance. Identification of precursors is the most probable method.

2. An accurate prediction of solar proton + HZE events based on solar parameters should be developed. It should give order-of-magnitude or better definition of the intensities and energy spectra. Timing is of concern.

3. Given an event on the sun, predict the evolution of an event from solar or interplanetary parameters.

4. Models of solar proton + HZE entry into the magnetosphere which include local-time and magnetic storm effects in rigidity calculations should be developed.

5. Determine the solar parameters which correlate well with the annual integrated fluences of unattenuated interplanetary protons + HZE with ~~energies above 10, 30, and 60~~ various energies in the range MeV, since sunspot numbers do not.

Research Areas in

2. Shielding Attenuation: spacecraft, spacesuits, body-self

a. 3-D analysis/evaluation of different geometries and materials
b. Optimization of shielding materials
c. Coordination and integration of:
   — research activities
   — data compilation (old & new)

B. Dosimetry

1. Development, testing of active and passive instruments (for space use) differentiating between high and low LET components of incident radiation at appropriate positions
2. Correlation and coordination of space information with ground based systems
3. Develop and design supporting (to active dosimeters) data reduction, interpretation, and transmission systems
4. Development of dosimetry supporting the ground-based radiobiology FOR REAL TIME READ OUT.
5. Explore microdosimetric techniques for measuring radiation quality in space
6. Study possible unique effects of very heavy (e.g. iron) particle tracks in crystalline structure

C. Expression of Dose for high LET radiation

Research is needed to evolve a new concept or unit relating particle fluence directly to radiation risk

Stanley Curtis
E. J. Stassinopoulos

I

A. Definition of Environment

1. ~~Definition of Primary Environment: The following areas:~~

a. Energetic Particles

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b. ~~5.2~~ Solar Flare Protons and Cosmic Rays

1. A predictive technique must be developed which will warn of anomalously large events (e.g., August 1972) hours or days in advance. Identification of precursors is the most probable method.

2. An accurate prediction of solar proton (+HZE) events based on solar parameters should be developed. It should give order-of-magnitude or better definition of the intensities and energy spectra. Timing is of concern.

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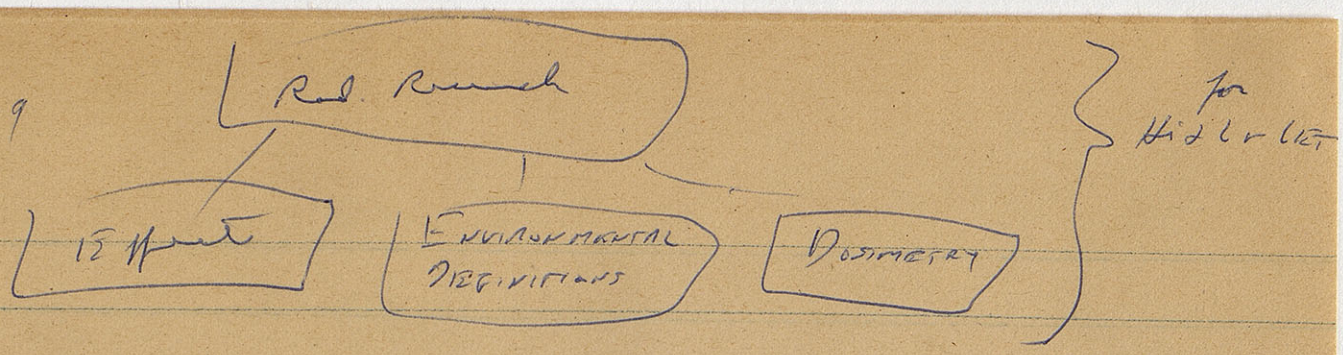
D
11-29-79



Dose Expression — Risk Units? Risk Equivalent Units?

Adequacy of Present Evaluation? — Rec

HZE (Hi Rate in Space (Beyond Belts) Galactic Background 8 or 10/cm²/Hr of LET?
Protons + Neutrons (Hi E) Inadequate shielding.

OUTLINE

I ENVIRONMENTAL PHYSICS
A DEFINITION
B DOSIMETRY
1. ACTIVE + PASSIVE IN SPACE.
COORD. + CORRELATION ± ground-based (GB)
2. INSTRUMENTATION IN SPACE
3. G-B TO RADIOBIOL.
4. MICRODOSIMETRY (OTHER DOSIMETRY NEEDS)
C. EXPRESSION OF DOSE (Hi LET PARTICLES) CONSIDER TO MEET PARTICLE RAD, REM, RBE etc. RISK EQUIV. UNITS, etc

II RADIATION BIOLOGY Hi LET EMPHASIS BUT NOT EXCLUSIVE
A. ANIMAL EXPERIMENTATION (PICKERING + SONNENHAUS)
1. G-B (EMPH. QUANTIFICATION)
a. LO LEVEL WHOLE BODY RAD. FOR EFFECTS (CA, TERATOGENESIS etc.)
b. SPECIFIC ORGAN (LOCAL + WHOLE BODY)
c. MECHANISMS OF EFFECTS (TISSUE, CELL, MOLEC.)
2. (cont.)

~~X~~ 2. Alert (Barnes & Me)

~~X~~ B. Human Studies (Barnes & Mr)

1. G-B

2. Alert — Retrospective & Prospective follow-up of cases, dosimetry, Histology etc.
Biological Indicators

III Operational Countermeasures (Rambaut & Wood)

A. Body Shielding

B. Work Rest Cycles

C. Radioprotective Chemicals

D. Warning Measures & Evasive Actions

E. Post-Exposure Amelioration

~~STF~~

IV Other

A. Training

B. Strong endorsement of continued support for Biomedical Facility for Space Related Research

C. Recommend additional Radiobiological Research using Radiation Exposure Facility committed to G/B Space Related Research.

D. Recommend periodic review & evaluation of "Space Radiation Protection Guidelines" in light of available information.

II RAD. BIOL.

B. HUMAN

1. GB

DATA RETRO & PROSPECTIVE ON HUMAN EXPOSURES (ALL AVAILABLE SOURCES). RE HZE, ETC DATA c̄ NCI (& ACCIDENT) STUDIES ON CONTINUING BASIS. ATTN TO DOSIMETRY.

ESTABLISH DOSE - RESPONSE DATA CORRELATION ~~DATA~~ FACILITY - COMPUTERIZED - CONTINUING. CENTRAL?

INFO MUST BE QUICKLY & EFFICIENTLY AVAILABLE - CALLS FOR CLOSE INTERAGENCY COMMUNICATION TIES.

2. ALOTT

ESTABLISH IMMEDIATE & LONG RANGE FOLLOW UP Hx, Px & Lab. EVALUATION SET ~~FOR~~ FOR CONTINUING ~~DOSE RESPONSE EFFECTS~~ FOR RETROSPECTIVE CORRELATION ON ALL SPACE FLIGHT PERSONNEL PRESUPPOSES STD. IN-FLIGHT DOSIMETRY - WELL & CAREFULLY ~~[illegible]~~ SELECTED.

DETAILED FLIGHT ENVIRONMENTAL, PHYSIOL. & INCIDENT DATA ON INDIVIDUALS FLIGHT OR FLIGHTS MUST ACCOMPANY ~~ASTRONAUT~~ FLIGHT PERSONNEL IN THEIR OWN FILES - R.O. OTHER POSS. ~~[illegible]~~ ETIOLOGIES FOR EFFECTS OBSERVED.

II Radiation Biology

A. Animal

2. Aloft

(1) Over-all Dose Response Studies
Specific Effects - Late
Life Shortening
'Early' - Sp. Organ / Whole Body

Dose-Response & Std. Specimens
Radiation Effects in Std. Animals (Std. Mouse, Rat, Primate)
c̄ Excellent + Std. Dosimetry.

Devel. of Std. Animals (Careful Selection + G/B Confirmation Studies)
Devel. of Acceptable Biochem. & Cell Response Techniques
Devel. of Std. Dosimetry - See Above I
Selection of Std. End Points for
Devel. of new End Points for Response Studies
- Sensitive Behav. Exams, Sens. Eye Studies, Genetic Studies etc.
Devel. of G/B Simulation Techniques for Proper Control Studies
Post Flt. G/B Studies c̄ Similar Specimens Exposing Grps. to Single Radiation Types & Simulated Combo - Det. Synergism
Repeat Exposures - Same Animals or Specimens (Fractionation)
Concurrent Animal Compared c̄ Man Responses.

~~2 Sp. Organ Effects~~
(2) Combined Effects — 0G + Radiation
Vary G Profiles

Mechanisms - Best Studied on Ground

AC 512 536 3414

Home

512 492-9480

Pick

Operational Countermeasures.

Body shielding

Ground based

- Application of current ~~cod~~ transport codes to evaluate various shielding configurations for variety of space radiation spectra and particle mixes
- Development of improved transport codes
- Development of organ shielding techniques
- Research into optimal designs for shelters
- Evaluation of prototype shielding concepts at accelerators that simulate space radiation

Aloft.

- Evaluation of prototype shielding concepts in flight

Radioprotectants

Ground Based

- State of Art review of radioprotectant literature with respect to high Z issue, particularly USSR data
- Expanded research to identify additional agents
- Research on effectiveness of combination therapy ie multiple drugs, nutritional concerns, other
- Basic research on structure-function relationships
- Research into chemicals that maintain immunity in case of high exposure
- Research on Risk/Benefit of radioprotectants

Aloft

- Drug distribution and utilization in the body at zero gravity
- In flight evaluation of radioprotectant performance if suitable endpoint can be defined

Amelioration

- Research into chemicals which when taken post radiation may modify effects.
- Influence of physical countermeasures on radiation effect.

M - Epidemiology

Outline for Research Topics

I. Specific Issues

A. Cancer

1. Leukemia
2. Thyroid
3. Other

a. Occupation
b. Background
c. Medical
d. Weapons
e. Nuclear Power
f. Nuclear Accidents

B. Other Somatic Effects (Late)

Interactions

C. Fertility, Genetics and Developmental

1. Chromosomal
2. Twinning
3. Duration of Risks
4. In utero exposure

II. General Issues

A. Dose Response

1. Massive Doses
2. Low Dose Acute-- High LET / Low LET
3. Variations for specific cancers
4. Host Factors
   a. Age
   b. Sex
   c. Race
   d. Health Status
4. Organ Sensitivity
5. Absolute and Relative Risk Models
6. Special & Hi-Risk Populations
7. Attributable Risk

B. Data

1. Cohorts and Controls
2. Dosimetry
   a. Cytogenetics
   b. Background
   c. Fractionation
   d. Dose Distribtuion
   e. Quality Factors

C. Dose Response Known

1. Hi-Dose (Acute) is carcinogenic
   (Est. of Dose-Response are "Good")

2. Hi-Dose (Chronic) is carcinogenic
   (Dose Response Poor for Low LET - Good for High LET)

3. These organs are sensitive for development of cancer
   a. Thyroid
   b. Bone Marrow
   c. Female Breast

4. Somewhat less sensitive
   a. Lung
   b. GI Tract
   c. Bone
   d. Skin

5. Some other organs

6. Other Somatic effects
   a. Cateracts
   b. Developmental defects
   c. Cytogenetic damage

7. Other relevant factors
   a. Age at exposure
   b. Sex
   c. Smoking (possible relations to latent period)
   d. Differing population susceptibility

D. Low level exposures

1. (Low - within current guides for occupational exposure, i.e., 5 rem per year or less)

2. Acute exposures (Single exposures)
   Suggestive - e.g., thyroid risks - less than $20/10^6$/yr/rem

3. Chronic exposures
   Suggestive - Radiologists (two-fold excess)

4. Other Somatic Effects
   None known

E. NEEDS:

1. Elucidation of dose response at low levels requiring--

   a. Large populations
   b. Doses well measured (i.e., within ±
      Rate
      LET
      Fractionation
      Distribution
   c. Range of doses
   d. Population can be followed over time--long term
      (20-25 years minimum)
   e. Multiple populations--to cover appropriate host factors

2. Legislation may be necessary to make this possible

F. CONFOUNDING FACTORS (which need to be controlled for)

1. Age--e.g., at first pregnancy
2. Race - Sex
3. Occupation
4. Other exposures--(radiation (e.g. medical)
   (chemicals (e.g., benezene)
5. Personal habits
   a. Smoking
   b. Alcohol consumption
   c. Diet
6. Medical history (other diseases)
7. Family history
8. Geography
   a. Mobility
   b. Residential history

G. POTENTIAL POPULATIONS (for exposure)

1. Now (presently under study)
   Hiroshima--Nagasaki
   Ankglosing spondylitics
   Medically exposed populations
   a. Women - cervical ca--etc.
   b. Tuberculosis patients
   c. Iodine I 131 (therapeutic and diagnostic)
   d. Thymic irradiation
   e. N-P
   f. Mastitis
   g. Thorotrast exposed
   h. Tinea capitis
   i. Ra 224 (Germany)
   j. Ra 226 (Chicago)

2. Occupationally exposed
   a. Dial painters
   b. AEC-DOE etc. Atomic workers (incl. shipyard workers)
   c. Underground miners
   d. Radiologists and technicians
   e. Military (DOD--e.g., "test" exposures)
   f. Thorium workers
   g. Phosphate ferticilizer workers (FLA.)

3. Environmentally exposed

   a. Utah (Lyons)
   b. Denver population
   c. Marshall Islanders

H. NEW POPULATIONS (Candidates)

"Badged" employees
  NRC
Utah "thyroid" cohort
Free-living populations (high background but serious dose problems)
  e.g. a. Kerala
       b. China
       c. Normany-Brittany
       d. Andes
       e. Brazil

2. Accidentally exposed populations
   Windscale workers
   Peri-Uranium tailings populations
   e.g. a. Cannonsburg, Pa.
        b. Grand Junction, Colo.
        c. Middlesex (?), New Jersey

3. High altitude flyers
   e.g. a. astronauts
   b. flight attendants--pilots, etc.

Strategic Projection Papers

Assignments:

Procedure

a. Plans are to send Genevieve Matanoski copies of scientific paper sections as written by group members

b. Sam Marcus will send copy to Warren Winkelstein to get his input for corrected report.

Cross-cutting questions (author)

Jablon--Schneiderman
Legal Issues

Science Projection--General Coordination -- Matanoski

State of the Art (known and unknown)
Matanoski

Populations--Industrial, etc. (old)
Lushbaugh

Confounding and dose response
Boice--Beebe

Populations--Medical
Boice

Natural Background
Masse'

Dosimetry--(except for cytogenetics)
Matanoski

Dosimetry--Cytogenetics
Lushbaugh

CROSS CUT ISSUES

1. Identification of studies with potential yield
   -- minimum standards
   -- credibility of studies done
2. Public perception of hazards
   -- public (and other "open") participation
   -- disinterested scientific oversight
3. Coordination of Studies
   -- NIH as science monitor?) Place of Federal Interagency
   -- Non-science issues - by whom?) Committee ?
   Identification of areas of need and priority

4. Support
   Continuity - and mechanisms (grants, contracts, "In house")
   Trained personnel
   Allocation - New vs. old
   Institutionalization (who does it? what else do they do?)
   Research Funding

5. Laboratory - Epidemiology Interactions
   Structural issues
   Joint workshops - multidisciplinary projects

   Lab to man:
   DNA repair
   Enzymology
   Immune phenomena
   Repair mechanisms

   Man to Mouse (lab)
   Dose response in "mixed" population
   Breeding "non-susceptible" animal
   (to parallel human response levels)
   Age at exposure effects
   e.g., mouse equivalent of in-utero exposure in humans
   Interaction studies
   Cardiovascular (and other measurable end points--"Behavioral toxicology")
   Mesothelial growth patterns

6. Legal (and other) problems in data access

   --confidentiality
   --who "owns" data collected with public funds
   --Social Security and IRS data
   --Extension of National Death Index
   --Incidence data--sources ?

Additional question:

What mechanism can be developed for evaluation of data collected as as a result of public funding with particular reference to access to raw data and an opportunity to carry out parallel analyses?

11-29-79

Suggestions for Cross Cutting Questions

Meeting to Develop
the Federal Strategy for Research into the
Biological Effects of Ionizing Radiation

1. What are the benefits to man of controlled (medical or other) uses of ionizing radiation?

2. What do we know "for sure" about the adverse effects to man of "low" doses of ionizing radiation? (background to 5 rad/year) (high and low LET)

3. What do we know about the adverse effects to man of sublethal (e.g., 5-100 rad) of ionizing radiation (high and low LET)?

4. What are the known or likely effects in man of ionizing radiation exposures on future generations?

5. To what extent are we justified in extrapolating from experimental systems (cell cultures - animal experiments) to the human population? What animal systems are most representative of the various human situations? (What are the limits of applying animal data to humans?) What are the limits of permissible human experimentation? What are the limits of epidemiological studies in defining the risk(s) of low-level ionizing radiation? What "sub-populations" (naturally occurring, occupational, or clinical) are potentially available for studies of the biological effects of ionizing radiation in man (low-level or otherwise)?

6. What is known about the effects of differences in schedules of delivery of a given dose of ionizing radiation (dose rate, fractionation) and "quality" of radiation (LET) on the biological response in animals and man? How does this extrapolate to the effects of low doses?

7. What do we know of the effects of other agents (physical and chemical) on the responses of biological systems (cell cultures, animals or man) to ionizing radiation? Should "permissible" radiation exposure levels consider possible radiation-modifying circumstances at the work place and elsewhere? (Also, should individual variations in susceptibility to radiation effects be taken into consideration, if these can be established by objective tests?) (This latter consideration would also be of importance for selection of operating personnel in nuclear power plants, space travel and work outside the earth's atmosphere.)

8. How dependent should radiation protection ("acceptable" exposure limits) be on the assumption of a given dose-versus-effect model for the estimation of potential risk? What studies (physical, chemical or biological) are needed to establish the nature of the dose-versus-response curve of low radiation levels, for different end points (both for low- and high-LET radiation)?

9. What can be done to protect the human population at large against [the effects of] ionizing radiation (environmental, workplace, clinical exposures; external

radiation, as well as internal emitters)? (Physical and chemical protection, dose reduction, disposal, decontamination, post-exposure therapy?)

10. What information should be available to the public to allow a meaningful discussion relating to regulation of non-therapeutic exposures to ionizing radiation? How should this information be made available, and who should be responsible for making it available? (Should life-shortening be used as criterion instead of [or in addition to] increase in cancer incidence? Presentation of estimated absolute and/or relative increase in risks, relative to other everyday risks.) Should a case be made for the acceptance of a "de minimus" approach whereby one would decide to ignore exposures that would add an increment of radiation exposure less than the standard derivation of the background radiation level throughout the USA (i.e., ignore doses less than 10 mrem/year)?

Cluster B* Chairman: Dr. Warren Sinclair

A. SOURCES, PATHWAYS, ETC.

I. Natural Radiation J. Hunds *all consultants present

1. Radon & Thoron

Survey measurements in homes, buildings, workplaces (as a function of time, and estimate doses).

Measurement techniques for Thoron and Daughters

2. External Gamma Rays from Building Materials

Further identification of sources of radiation in building materials (marble in Boston's South Station).

3. Airplane Travel

Measurement of doses to passengers and crew.

4. Radioactivity in Drinking Water (Surveys - realistic standards)

II. OCCUPATIONAL EXPOSURE E. Webster

1. Improved personnel measurement techniques, especially neutrons (cf. limit of detector at 10mR or less).

2. Relationship between surface dose measurement and estimated dose to organs of individual.

3. Metabolism of radionuclides in worker, es pecially after inhalation of Put Th (form is very important).

4. Special study of the "high dose" group of workers.

5. Identification of purpose of personnel monitoring system in relation to retrospective epidemiological studies.

III. RELEASES TO THE ENVIRONMENT Bjärngard

1. Is monitoring adequate for accidental releases from all sources?

2. Waste Management: a) incineration, and b) accelerated life testing for solid high-level waste disposal.

IV. EXPOSURE IN HOME FROM CONSUMER PRODUCTS Bjärngard

1. Radon

Rapporteur: J. Root

2. Important area to monitor technology developments - (especially NARM materials); also tritium in watches.

V. TRANSPORTATION OF MATERIALS INCLUDING ACCIDENTAL RELEASES

1. Monitoring methods intrinsically sound, but monitors not always available where needed (also shielding).

2. Models for accident situation - adequate?

3. Emergency plans.

VI. EFFECTIVE ENERGY STRATEGIES Gregg

1. Effects of improved insulation-ventilation.

2. Effects of increased coal burning; releasing more radioactivity (?geothermal).

3. Underground home

4. Radioactive products from fusion (Tritium released to space?).

B. REDUCTION OF EXPOSURE

I. Occupational Webster

1. Other Modality Research (structure testing, etc.)

2. Better shielding of radiographers and radiologists.

3. Identification of occupations with poor protection practices (e.g., industrial radiographers) and taking appropriate action.

II. Improvement of Medical Techniques Schneider

1. Dose optimization in treatment planning.

2. Quality Assurance: Investigate systems analysis and apply to individual clinical situations.

3. Development of dose reduction technology

   a) Improve Contrast Agents
   b) " Detector Efficiency
   c) " Image-Processing Procedures
   d) " Source Spectra
   e) " Scatter Rejection
   f) " Resolution (System MTF)
   g) " Low Attenuation Materials

4. Early detection of cancer

5. Other modalities (ultrasound, NMR, thermography, microwaves)

6. Medical cyclotron development for short-lived isotopes

III. Improvement of Waste Management Procedures (Gregg)

C. MEASUREMENT AND DOSIMETRY*

I. Measurement and Instrumentation

1. Improve low-dose high-LET measurement procedures (low dose-high dose rate)

2. Application of measurement techniques to retrospective exposure estimation

3. Dosimetry applicable to biological significance (fundamental considerations)

II. Measurement and Prediction of Dose Distribution

1. Improved modeling for dose distribution situations

2. Assessment of whole-body dose in partial-body exposures (tinia capitis ankylosing spondylitis)

III. Internal Emitters Dosimetry

1. Hot particle dose specification

2. Organ dose distribution and metabolism

DN:fcr
11-7-79

* Loevinger & Schneider

Outline for Research Topics

I Fundamental Scientific Questions.

A. Multidisciplinary in nature-require mathematics, physics, chemistry, and biology together at most basic level.

1. Radiation effects are a perturbation of the normal biological system-one must study normal and perturbed systems.

2. To understand complex biological systems one needs to understand the much simpler atomic and molecular processes both normal and perturbed.

3. One of the roles of physics, after understanding and quantitating simple systems, is to synthesize logical models which describe behavior of more and more complex biological systems.

B. Physics research essential to progress in biological effects of radiation.

1. Primary energy transfer from radiation to matter, especially condensed matter.

2. Time sequence and spatial distribution of secondary radiation-induced events.

3. The progression of these radiation-induced events into the molecular damage, reflected biologically.

4. Effects on the above process due to physical differences between various kinds of radiation.

5. Complete understanding of these phenomena will require input from diverse fields of physics, atomic physics, molecular physics, nuclear physics, thermodynamics and statistical physics, kinetics, physics of condensed matter,...

C. Physical characterization of radiation exposure

1. Conceptual translation of above fundamental information to biologically relevant parameters. Present dosimetry system, based on absorbed dose and LET, needs improvement or replacement.

2. Improvement of dose distribution information, including radiation quality, inhomogeneities, tissue variations, and size of domain including micron and submicron levels.

3. Special problems of internal radionuclide dosimetry.

II Applied Physics and Technology

A. Radiation Sources.
New radiation sources are becoming important, e.g. heavy ions, synchrotron radiation, pi mesons, exotic particles, space radiations.

1. New protection problems
2. New research opportunities
3. New therapeutic and diagnostic applications

B. Dosimetry.

1. Improved dosimetry methods and instrumentation.

a. Solid state dosimetry, passive and active
b. Chemical systems.
c. Improvement of traditional systems, e.g., calorimetry, ionization.
d. Search for new systems, e.g., lyoluminescence, liquid xenon.
e. Biological dosimetry methods.
f. Biophysical; analysis of exposed biological systems.
g. Indirect methods of dosimetry, e.g., spectroscopy.
h. High time resolution dosimetry methods.
i. Systems with similar response to biological systems.
j. Instrumentation for dose pattern measurement.
k. Technology of dose distribution calculations.

2. Problems where improved dosimetry is needed.

a. Personnel Monitoring-low energy neutrons, beta rays, low energy photons.
b. Dosimetry of radionuclides incorporated in the human body, location and quantification, e.g., plutonium particles in the lung.
c. Methods for population dosimetry-background levels, nuclear accident, medical exposures, civil defense.
d. Environmental dynamics of dose or activity distribution patterns-local and global.
e. Dosimetry of other environmental agents which may synergize with radiation.
f. Dosimetry for epidemiological studies retrospective and prospective.
g. Incorporation of dosimetry information into decisionmaking in various fields-radiation emergencies, risk estimation, medical patient management.
h. Improved radiation treatment planning.
i. Standardization and quality control of dosimetry measurements.

C. Physics Contributions to Radiation Applications

1. Diagnostic radiology

   a. CT scanning and imaging.

   b. Reduction of population dose through advanced imaging technology.

   c. Source improvements such as magnification radiography, heavy ion radiography.

2. Nuclear Medicine

   a. Three dimensional scanning.

   b. Time-dependent dynamic imaging.

   c. Use of radioactive beams.

   d. Use of fluorescent x-rays.

   e. Neutron activation methods.

   f. New in-vitro assay methods.

3. Radiation Therapy

   a. New Radiations-neutrons, heavy ions, pi mesons.

   b. Improvements in radiation treatment planning, e.g., 3-dimensional inhomogeneities, CT scanning, interactive therapy.

   c. Mixed modalities-high and low LET, chemical sensitizers, chemotherapy, surgery, hyperthermia.

   d. Modeling of biological data for radiation therapy.

4. Analysis of molecular and cellular structure

   a. Soft x-ray, electron and heavy ion microscopy.

   b. EXAFS-Extended X-ray Absorption Fine Structure.

   c. X-ray and particle fluorescence microanalysis.

   d. Auger and photoelectron spectroscopy.

   e. Small angle fast neutron scattering.

   f. Cytofluorinetry.

   g. Channeling and blocking of charged particles.

III Problems in the implementation of research of BEIR

a. Need for interdisciplinary approach-physical scientists should participate in planning, execution, and analysis of biological experiments.

b. Education of highly-qualified scientists for radiation physics and related multi-disciplinary fields should be stimulated by fellowships, postdoctoral appointments, etc.

Strategic Projection Papers

Assignments:

Editor: M. Inokuti

IA. Tobias and Auxier

IB. Turner and Inokuti

IC. Roesch

IIA. Tobias

IIB.1 Caswell

IIB.2 Auxier

IIC.1 Roesch

IIC.2 Tobias

IIC.3 Roesch

IIC.4 Inokuti

III Caswell

First draft to Inokuti (1)	December 1
Combined draft to members	December 20
Comments to Inokuti	January 10
Documents due	February 1

(1) Send also to group members

Outline for Research Topics

I. Beneficial Aspects of Radiation

Overview and Collation

Medical exposure to ionizing radiation is responsible for curing orders of magnitude more cancers than it produces. Such cancer cures come from diagnostic radiology and from radiation therapy. For example it has been estimated that radiotherapy is responsible, either totally or in part, for curing approximately 100,000 cancer patients in the United States per year. There are approximately 3/4 million former cancer patients who have been cured of their disease due to radiotherapy. Improvements in radiotherapy resulting from the research efforts listed below will lead to an additional significant reduction of the 100,000 cancer deaths due to lack of local control by current treatment methods in the United States. Improved diagnostic techniques combined with the optimum use of radiotherapy plus a systemic agent (eg. chemotherapy or immunotherapy) could lead to a further significant increase in cure rate. Against this beneficial use of radiotherapy the deleterious effects in terms of cancer production are very small, less than one in one thousand → cured patients.

The following outline addresses the broad research areas identified as ways to improve our ability to achieve improved cure of cancer, improved quality of life, and decreased cancer care costs.

A. Studies into biological mechanisms relevant to radiation response in tumors and in normal cells and tissues.

Design of optimum treatment and consequent improvement in cure rates will depend largely on our understanding of the interactions of ionizing radiation with biological materials at the sub cellular, cellular and tissue levels. Of special importance are the various repair processes. Improvement will also depend on better understanding of tumor biology, including the mechanisms of metastatic spread, tumor cell kinetics and differentiation, the relationship between stroma and the vascular system and the development of cells that are hypoxic, acidic and at low pH etc.

B. Conventional irradiation used alone for cancer therapy: time, dose, dose-rate, and volume effects on tumors and normal tissues.

1. Experimental

What determines biological responses to fractionated irradiation of tumor and normal tissues (eg reoxygenation, repair, repopulation, recruitment, etc.; what are target cells; new models for normal tissue injury).

2. Clinical

Evaluation of various fractionation schedules or dose-rate on tumor and normal tissue response.

a. tumor response

b. acute effects on normal tissues

c. late effects including carcinogenesis and teratogenesis

C. Heavy particles and other non-conventional radiation.

These may have advantageous physical and/or biologic properties.

1. Physical properties

   a. Improved dose distribution yielding higher tumor dose with decreased dose in normal tissue.

2. Biological properties

   a. Circumventing the protective effects of hypoxia in tumors

   b. Repair mechanisms

   c. Optimum fractionation schedules

   d. Late effects on normal tissues, including fibrosis, vascular changes, carcinogenesis, etc.

   e. Other

D. Modification of radiation response in tumors and normal tissues:

1. Chemical radiation sensitizers of tumors
2. Radiation protectors of normal tissues
3. Hyperthermia
4. Other physical modifiers

Increasing the tumor response with a radiosensitizer eg. Misonidazole, and/or decreasing the normal tissue response with a radioprotector eg. WR 2721 would increase the tumor cure rate. Similarly, localization of heat treatment to tumors would increase local control rates.

E. Combining treatment by ionizing radiation with other anti-tumor modalities:

1. Surgery
2. Chemotherapy
3. Hyperthermia
4. Immunotherapy
5. Other

For each of the above we need to understand the basic biology of the independent actions and interactions, the effect of sequencing and dose, possible effects on distant metastases and other factors. The goal of these adjuvant treatments (eg radiation + chemotherapy, and radiation + immunotherapy) is often to treat distant metastases, and therefore the need for a differential effect on normal and malignant tissues is not essential. However, interactions at the local site do occur, need to be understood, and may be used to enhance local control rates.

F. Tumor localization techniques in radiation therapy (cross cut with diagnosis)

1. External imaging systems
   a. Conventional X-ray
   b. CT scanning
   c. Ultrasound
   d. Microwave
   e. Nuclear magnetic resonance
   f. Heavy particles
2. Internal and external imaging systems
   a. Radionuclides, tumor seeking nuclides or complexes
3. Invasive localization procedures
   a. Intravascular catheterization and imaging

Outline for Research Topics

IDENTIFICATION OF AREAS OF RESEARCH IN RADIATION CHEMISTRY FUNDAMENTAL TO RADIATION BIOLOGY

Among all the environmental hazards that man is exposed to, ionizing radiation is the most thoroughly investigated and the most responsibly monitored and controlled. Nevertheless, much more information concerning the biological effects induced and their modifications and reversal is required. Together with radiation physics, an understanding of radiation chemistry is necessary for full appreciation of biological effects of high and low energy radiations and for the development of prophylactic, therapeutic, and potentiating methods and techniques in biological organisms. This group has identified the following general areas of radiation chemistry for which extensive support should be considered to realize these goals.

I. Very Early Time-Scale Events Preceding Chemistry

Relative importance of ionization, excitation, and charge recombination in model systems. Some of these processes can be studied only at the theoretical level; but attempts should be made to correlate with experimental studies. Such experimental studies will involve very early time-scale measurements.

II. Kinetics and Mechanisms of Free Radical and Excited State Reactions

A. Experimental approaches
   1. Steady state radiolysis and product analysis
   2. ESR techniques for radical studies
   3. Pulse radiolysis for characterization of properties of transients (absorption and emission spectroscopy, conductivity, fast ESR, light scatter, etc.)
   4. Chemistry of excited states as related to ionization processes and photo ionization (involving low and high energy protons).

B. Physico-chemical parameters
   1. Concentration of solutes in solvent ("direct" vs. "indirect" effects) and organization
   2. State of aggregation (micelles, membranes, liposomes, solid state systems)
   3. Oxygen effects (peroxy radicals, super oxide radical, peroxides, etc.)
   4. Electron transfer between and within biomolecules and model systems.

III. Modifiers of Radiation Biological Effects

A. Enhancement
   1. Radiation sensitizers in, and relation to, radiation therapy (redox sensitizers, anti-cancer drugs, cyanide release, synergisms)
   2. Metal ions.

B. Protection
   1. Chemical restitution (electron, charge and H atom transfer)
   2. Effects of antioxidants and nutrients.

IV. Problems in Applying Radiation Chemistry to Radiation Biology That Must Be Resolved

A. Very high dose rates within pulses not normally encountered in radiation biology
B. Single pulses, usually used in pulse radiolysis--perhaps not applicable to radiation biology (repetitive pulse studies required)
C. Application of knowledge from nonpolar systems required.

V. Large Instruments for Study That Should Be Generally Available to Scientific Public

A. Lasers (high power and various wave length)
B. Electron pulse accelerators
C. High energy particle pulse accelerators
D. Synchrotron orbital radiation.

At present, laboratories known to Cluster G that welcome outisde users are:

1. BEVALAC, Lawrence Berkeley Laboratory, Berkeley (particle pulses)

2. Center for Fast Kinetics Research, Austin (electron and laser photon pulses)

3. Synchrotron Orbital Radiation, Cornell.

Strategic Projection Papers

Assignments:

AUTHORS:	Section I	Chatterjee
	Section II	Burr
	Section III	Simic
	Sections IV and V	Powers

Final draft will be Powers and Simic.

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : Consultants

DATE: November 26, 1979

FROM : Dr. Charles U. Lowe, M.D.
Special Assistant to the Director

SUBJECT: Meeting on November 29, 1979

We are happy that you will be able to join us on November 29 for the purpose of helping to draft an important element of what will become a Federal Strategy for Research into the Biological Effects of Ionizing Radiation. On November 7, a large group of consultants convened at NIH for this purpose; however, it was realized that one or several important areas had been overlooked or were not adequately represented among the initial group of consultants. The meeting on November 29 is scheduled to help rectify this deficiency. The group that will convene will address the research needs relating to the biological effects of radiation in space, specifically those from high Z radiation.

To give you a better appreciation of what the overall effort entails, we are enclosing a copy of the letter mailed to the consultants who met with us on November 7. The accompanying material from our meeting contractor, CSR, Incorporated, is of course pertinent to your convening at NIH on November 29.

Enclosures

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

October 26, 1979

Dear:

The Secretary, HEW, is required by law (P.L. 95-622 as amplified by supporting statements in the Congressional Record, October 14, 1978) to develop a comprehensive strategy for research into the biological effects of ionizing radiation supported or conducted by the Federal government. This strategy must reflect not only the needs of agencies with mandates to develop new knowledge, but also that research required by regulatory agencies to meet their responsibilities for protecting the public health. The Secretary has delegated this responsibility to Dr. Donald S. Fredrickson, Director of the National Institutes of Health.

This demanding and challenging responsibility requires the involvement of all Agencies and Departments having relevant programs. Accordingly, the Secretary chartered a committee chaired by Dr. Fredrickson, to act as a focal point in discharging this obligation. The Committee on Federal Research Into the Biological Effects of Ionizing Radiation has membership drawn from twelve Departments and Agencies, and has begun the process of formulating the Federal strategy.

While the Congressional intent was to limit the strategy to Federally funded or conducted programs, the Committee realized early in its deliberations that the success of the undertaking would depend in large part on its ability to recruit the advice and assistance of a large number of scientists pursuing their research in institutions of higher learning, private and public laboratories, and in private sector industry. Accordingly, a schedule of activities evolved to permit an interplay between these scientists and Federal officials.

On November 7 we plan to convene a selected group of scientists to consult on the drafting of an outline of research strategy that will be further developed by the Committee. The consultants have beeen chosen because they have an incisive grasp of a well defined area of research and, in many instances, a broad and comprehensive understanding of research issues as they intersect with public policy, consumer concerns, and political realities.

A preliminary and abbreviated outline of research has been developed by the Committee and contains twelve primary elements forming fairly well defined disciplinary clusters. The outline may provide no more than a starting point for discussion and need not be accepted in either form or substance. Approximately six consultants will be asked as a group to review a single element of this outline for organization, completeness, relevance, scientific opportunity, and the need for research supported by public funds. By the end of the day, we would expect to receive from each group of consultants a relatively detailed compilation of the research agenda they would recommend for Federal support.

From each group of consultants we expect to seek authors for what we have chosen to call "Scientific Projection Papers." These documents may be prepared by single authors or developed collaboratively. Some groups might choose to suggest the name of a scientist who may not have participated in the meeting on November 7 to write the "Projection Paper." The number of "Scientific Projection Papers" needed will vary among the disciplinary areas. We would expect advice on the requisite number.

The "Scientific Projection Papers," oriented toward disciplines, must have as a primary goal a justification for inclusion of the subject matter in a Federal research portfolio. They should be neither a "state of the art" summary nor a compendium of relevant science. Rather, we would expect a carefully reasoned document, placing the particular element of research into perspective, identifying the needs and opportunities, defining scientific questions to be answered, and the relation of this aspect of research to the larger total. At present, we cannot be precise about length, but we do not expect to receive voluminous documents. Ten to twenty typescript pages should suffice.

A limited number of papers of another sort will also be sought. These will be "issue papers" traversing a number of disciplines encompassing not only science related to the biological effects of ionizing radiation, but also the interplay between this body of knowledge and the need for and development of public policy. In addition, they should articulate, whenever appropriate, those problems which research alone cannot solve and must rely on the political process for resolution. This group of "issue papers" will serve to frame the scientific process, delineating both its strengths and limitations, and indicate how research can illuminate and guide the formulation of public policy. It seems particularly important to address matters which are of immediate concern to the public. The Committee will have selected the topics for "issue papers" in advance of November 7, but consultants may feel free to add additional titles.

All papers must be completed by February 1, 1980. These will be collated, printed, and be made available to the scientific community and to the public after February 20.

On March 10-11, we will convene an open meeting at which time the overall strategy will be discussed publicly. Authors of papers will be asked to present a synopsis of their recommendations, and the audience (Committee members, consumers, public interest groups, public administrators and scientists) will have an opportunity to comment, challenge or bless.

The product of this meeting should provide the essential material needed by the Committee on Federal Research Into the Biological Effects of Ionizing Radiation to fashion a well-groomed "Draft Federal Strategy." This "Draft" will be forwarded to a committee of the National Academy of Sciences for review on or before May 1, 1980. The Academy has a sitting committee reviewing current Federal research into the biological effects of ionizing radiation and will thus be uniquely prepared to provide a critique of the "Draft Federal Strategy." Within two months, the Academy Committee will return the "Draft" with comments, at which time the Committee will consider further recommended changes and modifications. It will be submitted in final form to the Secretary, Department of Health, Education, and Welfare for transmittal to the Congress by December 31, 1980.

This letter carries with it an expression of appreciation from the Committee and its chairman Dr. Donald S. Fredrickson. We are pleased that you have agreed to consult on this very demanding responsibility.

Should you have any questions, please feel free to contact me (301-496-3283) or my associates whose telephone numbers are noted at the bottom of this letter.

Sincerely,

Charles U. Lowe

Charles U. Lowe, M.D.
Special Assistant to
the Director

Dr. Oddvar F. Nygaard
Special Assistant to the Director
National Cancer Institute
301-496-9326

Dr. Elliott H. Stonehill
Research Planning Officer
National Cancer Institute
301-496-9326

CSR, Incorporated
805 15th Street, N.W., Suite 500
Washington, D.C. 20005
(202) 638-7620

November 26, 1979

TO: Consultants

FROM: Jeanne Seferovich
Conference Manager

SUBJECT: Meeting to Develop the Federal Strategy for Research Into the Biological Effects of Ionizing Radiation
November 29, 1979
National Institutes of Health, Bethesda, Maryland

CSR, Incorporated, under contract with the National Institutes of Health, will be providing the logistical, administrative, on-site conference support and expense reimbursement for the November 29 meeting. It is scheduled to begin at 8:30 a.m. in Conference room 5A-16, fifth floor of Building 31, "A" wing, and will conclude at approximately 4:00 p.m.

Reimbursement Information

Government regulations prohibit reimbursement to Federal employees attending Federal meetings. All Federal employees should consult their particular agencies regarding reimbursement for travel and per diem expenses.

Under the limitations of Federal reimbursement guidelines, all non-Federal consultants will be reimbursed by CSR, Incorporated for local and long-distance travel expenses, plus the actual cost of lodging and meals not to exceed $50.00 per day for overnight travel and an honorarium of $100 per day. A voucher is enclosed along with detailed instructions concerning allowable expenses. Should you need assistance in completing this voucher, CSR staff will be available at the meeting to answer any questions you may have. Following the meeting, please send the completed voucher to my attention at the above address. You may expect payment from CSR, Incorporated three to four weeks following receipt of your voucher.

Hotel Information

A room reservation has been made for all out-of-town participants at the Bethesda Holiday Inn, 8120 Wisconsin Avenue, Bethesda, Maryland. The daily rate for a single room is $43.00 (plus 10% tax).

If you guaranteed your room reservation for late arrival and your plans change, you must cancel your reservation by 6:00 p.m. on your scheduled day of arrival or you will be charged and billed directly for the room. The telephone number of the Bethesda Holiday Inn is (301) 652-2000.

Transportation

Limousine transportation to the Bethesda Holiday Inn is provided by Greyhound Airport Limousine from both Washington National and Dulles International Airports. The National Airport Limousine leaves from the main terminal, United Airlines entrance, and from the main entrance at North Terminal every 25 and 55 minutes past the hour. The fare is $4.75. The Dulles Airport Limousine leaves from the Arrivals (Lower) Level at all entrances at 30 minutes past the hour. The fare is $4.50

Greyhound Limousine Service runs daily from the Bethesda Holiday Inn to both airports. The limousine to National Airport leaves the hotel each day at 10 minutes past the hour from 6:00 a.m. to 8:00 p.m. The trip takes approximately 45 minutes and costs $4.75. The limousine to Dulles International Airport leaves the hotel Monday thru Friday at 40 minutes past the hour from 6:40 a.m. until 4:40 p.m. Travel time is estimated to be one hour, and the cost is $4.50.

Taxi service is also available from both National and Dulles Airports at rates of $15.00 and $25.00 respectively.

If you are driving to the NIH Camus and need a parking permit, please call me at the above telephone number.

CSR staff will be available on-site, November 29, to assist in coordinating all participant travel arrangements including confirming return airline reservations and arranging for taxi service to area airports.

I look forward to meeting you. If further assistance regarding these arrangements is required, please call me.

Attachments: NIH map
Reimbursement Instructions and Expense Voucher
(for non-government employees)

CSR, Incorporated
805 15th Street, N.W., Suite 500
Washington, D.C. 20005
(202) 638-7620

October 26, 1979

TO: Scientific Consultants (Non-Federal Employees)

SUBJECT: Reimbursement of Expenses and Fees

Fees and reimbursable expenses for authorized work performed under contract may include: consultant/speaker/scientific expert's fees (or Honorarium), travel, lodging, meals, and other scientific expenses. These items are defined below:

A. Lodging and Meals - Overnight Travel

The actual cost of lodging and meals is reimbursed up to a normal designated limit of $50/day for overnight travel in the Washington, D.C. area. (Note that $50/day is not per diem rate. It is a ceiling on actual cost reimbursement. Also, $22.50/day is considered to be a maximum cost of meals by the Federal Travel Regulations. Costs over this amount should be justified.)

Please list all lodging and meal expenses daily in the proper area on your expense statements. Receipts are required for hotel bills, and all expenses over $10.00 and as listed in D below. NOTE: Funds expended for alcoholic beverages are not reimbursable.

B. Meals - Non-overnight Travel

For non-overnight travel more than 50 miles from home or office, the normally designated limit for meals only is $22.50. (NOTE: Again, this figure is a ceiling on actual cost reimbursement, not a per diem rate.) Consultants who fall into this category should fill out a regular expense statement listing meal expenses in appropriate areas by date of travel.

C. Transportation Expenses

1. While in travel status, your actual transportation expenses are reimbursable, within the limits described below. Please attach receipts for expenditures in excess of $10, except for private automobile mileage. The more common reimbursable expenditures are:

   a. Air and train transportation at less than first class accommodations. Only if less than first class accommodations are not available or are inadequate may first class accommodations be utilized.

   b. Automobile mileage will be reimbursed at the rate of $0.17/mile plus cost of parking fees and bridge, road, and tunnel tolls. However, the total cost may not exceed the cost of travel by common carrier.

   c. Taxicab and airline limousine fares to and from terminals (tips are not reimbursable), mileage for use of car from home to terminal and for return plus parking. Limousines should be utilized when available except when taxi fare is comparable to limousine charges and it becomes a matter of convenience rather than cost.

   d. Taxicab, bus, or auto expenses to procure meals when the nature and location of the work at a temporary duty station are such that suitable meals cannot be obtained there.

   e. Rental cars when more economical than other available means of transportation.

2. With regard to transportation, consultants/speakers/scientific experts should make their own travel arrangements. CSR Incorporated, may provide tickets in advance upon request. Your ticket receipt must accompany your expense statement.

D. Other Reimbursable Expenses

1. Tips - Only for handling government property.

*2. Business supplies: recording tapes, film, xeroxing, and other forms of reproduction. Receipt required.

*3. Secretarial services: Without exception, an itemized receipt must accompany this item indicating the name of the secretary or Secretarial Service firm, the number of hours worked, the dates of service, the rate paid and the total dollar amount of the services.

4. Business telegrams and telephone calls.

5. Postage - receipt required.

*6. Freight - receipt required.

E. Consultant Fees/Honorarium

The maximum allowable consultant fee (Honorarium) is $12.50/hour - up to $100/day.

Please take care to fill out your expense statement completely and accurately, sign it and attach necessary receipts before submission to CSR for payment.

---

* ADVANCE AUTHORIZATION MANDATORY.

Name: _____

Address: _____

_____

EXPENSE STATEMENT

FOR NON-FEDERAL EMPLOYEES

CSR, Incorporated
805 15th Street, N.W. Suite 500
THE SOUTHERN BUILDING
Washington, DC 20005

Project No. & Date: _____

_____

_____

_____

Itinerary			*Lodging	Meals			Total Lodging & Meals	*Air/Rail/ Car Rental Paid	Misc. (Listed Below)	Paid Expenses Daily Total
Depart Date/Time	Arrive Date/Time	Destination		Breakfast	Lunch	Dinner				

* Receipt required

CONSULTANT FEE/HONORARIUM (Sign Other Side as Applicable):

Date	Place	Days/Hours	Rate	Amount

CSR Pre-Paid Items	
Air/Rail/ Car Rental	Ticket Number

SUMMARY:

Total CSR Pre-Paid: _____

Paid Expenses: _____

Less Cash Advanced: _____

Fee/Honorarium: _____

Total to be Paid: _____

MISCELLANEOUS EXPENSES (Mileage, Parking, Tolls, Bus, Taxi, Phone):

Date	Item	Amount

I certify these expenses correct.

Signature: _____

Social Security Number: _____ Date: _____

Approved: _____

Services Provided: _____

INSTRUCTIONS FOR COMPLETION OF EXPENSE STATEMENT

1. The headings of the form must be complete including name (last name first). If not a CSR employee do not fill out project number and date.

2. Receipts are required for all asterisk items and for any expense exceeding $10.00.

3. Miscellaneous expenses must be itemized.

4. Reimbursement is for actual expenses so be sure to include all monies spent, in detail.

CONSULTANTS

When you perform work under a contract while on annual leave or compensatory time from an agency or organization supported with federal funds, you must concurrently with the filing of your invoice for payment, certify that:

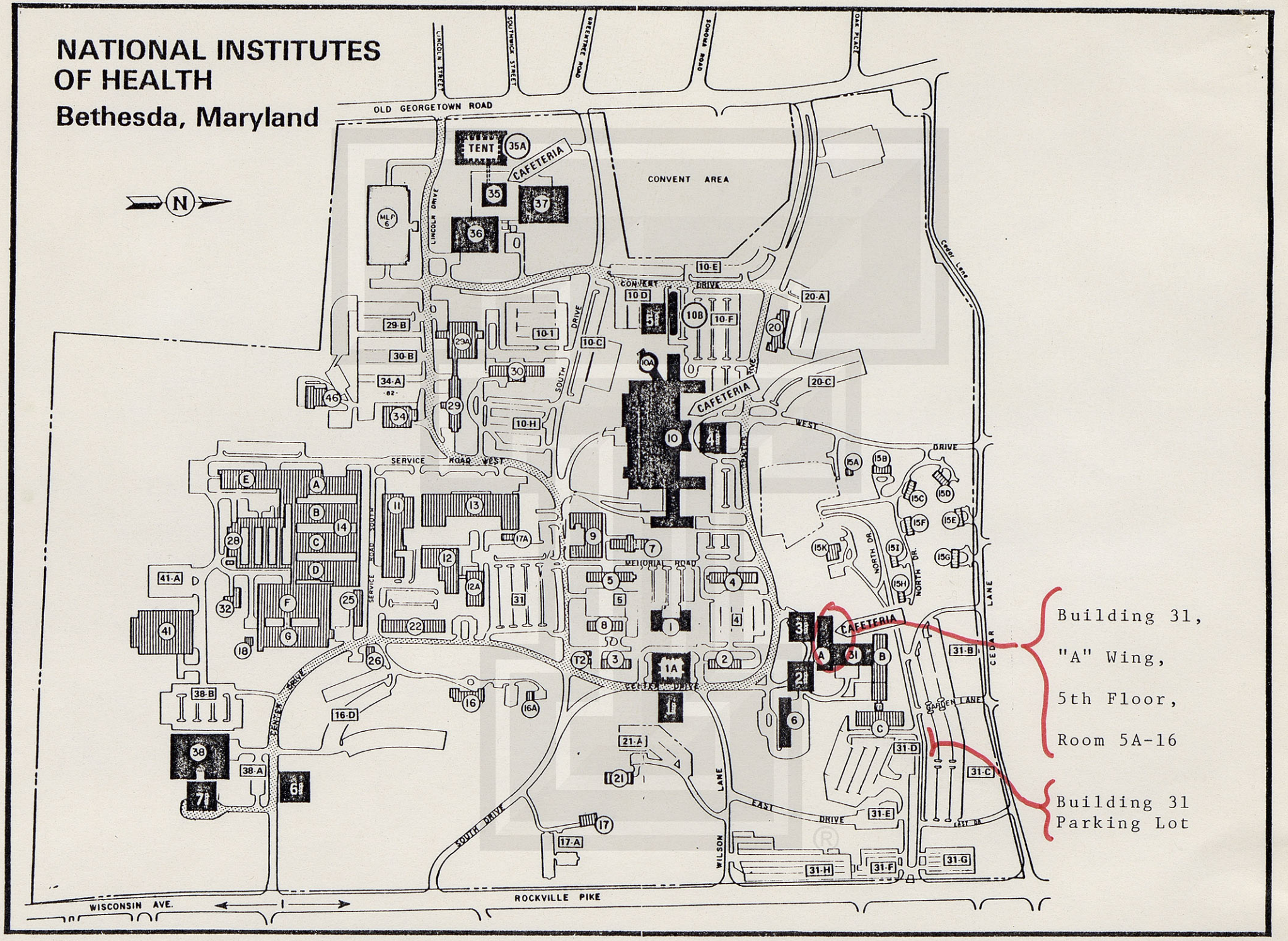
"The work or a portion of the work for which payment is requested was performed while on authorized annual or compensatory leave from an agency or organization supported with federal funds, and was performed with the knowledge of that agency or organization."

_____
Signature

_____ _____
Social Security Number Date

NATIONAL INSTITUTES OF HEALTH

Bethesda, Maryland



Building 31,
"A" Wing,
5th Floor,
Room 5A-16

Building 31
Parking Lot

COMMITTEE ON FEDERAL RESEARCH
INTO THE BIOLOGICAL EFFECTS OF IONIZING RADIATION

Chairman

Dr. Donald S. Fredrickson
Director
National Institutes of Health
Building 1, Room 124
Bethesda, Maryland 20205
301-496-2433

Executive Secretary

Dr. Joseph G. Perpich
Associate Director for
Program Planning and Evaluation
National Institutes of Health
Building 1, Room 137
Bethesda, Maryland 20205
301-496-3152

DEPARTMENT OF AGRICULTURE

Dr. Donald A. Lindquist
Science and Education Administration -
Agricultural Research
National Program Staff
U.S. Department of Agriculture
Bldg. 005, Room 207A - BARC West
Beltsville, Md. 20705
301-344-2771

DEPARTMENT OF COMMERCE

National Bureau of Standards

Dr. Chris E. Kuyatt
Acting Director
Center for Radiation Research
National Bureau of Standards
Building 245, Room C-229
Washington, D.C. 20234
301-921-2551

DEPARTMENT OF DEFENSE

Capt. Paul E. Tyler, MC, USN
Director
Armed Forces Radiobiology Research
Institute
National Naval Medical Center
Building 42, Room 2155
Bethesda, Maryland 20014
301-295-1211

DEPARTMENT OF DEFENSE(Cont.)

Lt. Col. Bruce A. Mazat, MC, USA (Alt.)
Deputy Director
Armed Forces Radiobiology Research
Institute
National Naval Medical Center
Building 42, Room 2155
Bethesda, Maryland 20014
301-295-1211

Col. Phillip E. Winter, MC, USA
Military Assistant for Medical
and Life Sciences
Office of the Under Secretary of
Defense for Research and Engineering
Pentagon, Room 3D129
Washington, D.C. 20301
202-697-8535

Lt. Col. Edwin T. Still, VC, USAF
Biomedical Advisor
Defense Nuclear Agency
Washington, D.C. 20305
703-325-0459

DEPARTMENT OF ENERGY

Dr. Charles W. Edington
Deputy Director
Office of Health and Environmental
Research
Office of Environment (E201)
Department of Energy
Washington, D.C. 20545
301-353-3251

Dr. William W. Burr
Director, Office of Health and
Environmental Research
Department of Energy E201
Washington, D.C. 20545
301-353-3153

DEPARTMENT OF HEALTH, EDUCATION,
AND WELFARE

Office of the General Counsel

Ms. Mary Pendergast
Office of the General Counsel, DHEW
Parklawn Building, Room 7-66
Rockville, Maryland 20857
301-443-8584

Office of the Assistant Secretary for Health

Dr. James F. Dickson III
Senior Advisor
for Environmental Affairs, OASH
HHH Building, Room 701H
Washington, D.C. 20201
202-245-6811

Dr. Lowell T. Harmison
Senior Advisor
Office of Enviornmental Affairs, OASH
Parklawn Building, Room 17A-55
Rockville, Maryland 20857
301-443-2650

Office of Health Research, Statistics, and Technology

Dr. Paul E. Leaverton
Associate Director for Research
Office of Statistical Research
National Center for Health Statistics
Federal Center Building, Room 212
3700 East-West Highway
Hyattsville, Maryland 20782
301-436-7135

Center for Disease Control

Bureau of Epidemiology

Dr. Clark W. Heath, Jr.
Director, Chronic Diseases Div.
Bureau of Epidemiology, CDC
Building 1, Room 5112
Atlanta, Georgia 30333
8-236-3961

Dr. Glyn G. Caldwell
Chief, Cancer Branch
Chronic Diseases Division
Bureau of Epidemiology, CDC
Building 1, Room 5112
Atlanta, Georgia 30333
8-236-3963

National Institute for Occupational Safety and Health

Dr. John R. Froines
Deputy Director, NIOSH
Parklawn Building, Room 8-05
Rockville, Maryland 20857
301-443-1530

Food and Drug Administration

Bureau of Radiological Health

Mr. John C. Villforth
Director
Bureau of Radiological Health, FDA
12720 Twinbrook Parkway, Room 501
Rockville, Maryland 20857
301-443-4690

Dr. Charlotte Silverman
Deputy Director
Division of Biological Effects
Bureau of Radiological Health, FDA
12709 Twinbrook Parkway, Room 101
Rockville, Maryland 20857
301-443-2356

National Institutes of Health

National Cancer Institute

Dr. Arthur C. Upton
Director, NCI
NIH Building 31, Room 11A52
Bethesda, Maryland 20205
301-496-5615

National Institute of Environmental Health Sciences

Dr. David P. Rall
Director, NIEHS
P.O. Box 12233
Research Triangle Park, N.C. 27709
8-629-3201

ENVIRONMENTAL PROTECTION AGENCY

Dr. David M. Rosenbaum
Deputy Assistant Administrator
for Radiation Programs (ANR-458)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
703-557-9710

Dr. William A. Mills
Director, Criteria and Standards Division
Office of Radiation Programs (ANR-460)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
202-557-0704

Dr. William H. Ellett (Alt.)
Chief, Bioeffects Analysis Branch
Criteria and Standards Division
Office of Radiation Programs (ANR-460)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
202-557-9380

Dr. George Simon
Health Effects Division
Office of Health and Ecological
Effects (RD-683)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
202-245-3025

NUCLEAR REGULATORY COMMISSION

Mr. Saul Levine
Director
Office of Nuclear Regulatory Research
Nuclear Regulatory Commission
Washington, D.C. 20555
301-427-4341

Dr. Robert J. Budnitz
Deputy Director
Office of Nuclear Regulatory Research
Nuclear Regulatory Commission
Washington, D.C. 20555
301-427-4338

VETERANS ADMINISTRATION

Dr. Lawrence Hobson
Deputy Assistant Chief Medical Director
for Research and Development
Veterans Administration
810 Vermont Avenue, N.W., Room 644E
Washington, D.C. 20420
202-389-2616

Consulting Members

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

Dr. Charles M. Barnes
Radiological Health Scientist
Medical Sciences Division
Lyndon Johnson Space Center (SD5)
Houston, Texas 77058
8-525-5281

NATIONAL SCIENCE FOUNDATION

Dr. Arthur Kowalsky
Program Director for Biophysics
Division of Physiological, Cellular,
and Molecular Biology
National Science Foundation
1800 G Street, N.W., Room 329
Washington, D.C. 20550
202-632-4260

Liaison Member

Dr. Howard E. Clark
(Chairman, Task Force on Biological
Effects of Non-ionizing Electro-
magnetic Radiation)
National Telecommunications and
Information Administration
1800 G St., N.W., Suite 760
Washington, D.C. 20504
202-377-1850

Subcommittee to Develop Federal Strategy for Research
into Biological Effects of Ionizing Radiation

Dr. Donald S. Fredrickson, Chairman
Director
National Institutes of Health
Building 1, Room 124
Bethesda, Maryland 20205
(301) 496-2433

Mr. Frank Arsenault
Director
Division of Safeguards and
Environmental Research
Office of Nuclear Regulatory Research
Nuclear Regulatory Commission
Washington, D.C. 20555
(301) 427-4350

Dr. Monte Blau
Veterans Administration
Medical Center
3495 Bailey Avenue
Buffalo, New York 14215
8-432-9011 x583

Dr. Glyn G. Caldwell
Chief, Cancer Branch
Center for Disease Control
Bureau of Epidemiology
1600 Clifton Road, N.E.
Atlanta, Georgia 30333
(404) 329-3961

Dr. Randall Caswell
Chief
Nuclear Radiation Division
National Bureau of Standards
Building 245, Room B-109
Washington, D.C. 20234
(301) 921-2625

Dr. Charles W. Edington
Deputy Director
Office of Health and Environmental
Research
Office of Environment
Room E-201
Department of Energy
Washington, D.C. 20545
(301) 353-3251

Dr. Charles U. Lowe
Special Assistant to the
Director
National Institutes of Health
Building 1, Room 103
Bethesda, Maryland 20205
(301) 496-3283

Mr. Sam Marcus
Special Assistant to the
Director
National Center for Health
Statistics
Federal Center Building
Room 2-19
3700 East-West Highway
Hyattsville, Maryland 20782
(301) 436-7019

Lieut. Colonel Bruce Mazat, MC
Deputy Director
Armed Forces Radiobiology
Research Institute
National Naval Medical Center
Building 42, Room 2155
Bethesda, Maryland 20014
(301) 295-1211

Mr. Melvin Myers
Director
Office of Program Planning and
Evaluation
National Institute for Occupational
Safety and Health
5600 Fischers Lane, Room 8A09
Rockville, Maryland 20857
(301) 443-4364

Dr. William Mills
Director
Criteria and Standards Division
Office of Radiation Programs
(ANR-460)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
(703) 557-0704

Subcommittee to Develop Federal Strategy for Research
into Biological Effects of Ionizing Radiation
(cont.)

Dr. Oddvar F. Nygaard
Special Assistant for Radiation
National Cancer Institute
National Institutes of Health
Building 31, Room 10A52
Bethesda, Maryland 20205
(301) 496-9326

Dr. Phillip Shambra
Associate Director for Interagency
Programs
National Institute of Environmental
Health Sciences
P.O. Box 12233
Research Triangle Park,
North Carolina 27709
(919) 541-3467

Dr. Charlotte Silverman
Deputy Director
Division of Biological Effects
Bureau of Radiological Health
Food and Drug Administration
12709 Twinbrook Parkway, Room 101
Rockville, Maryland 20857
(301) 443-2356

Lieut. Colonel Edwin T. Still, VC, USAF
Biomedical Advisor
Defense Nuclear Agency
Department of Defense
Washington, D.C. 20305
(703) 325-0459

Dr. Elliott H. Stonehill, Executive Secretary
Research Planning Officer
National Cancer Institute
National Institutes of Health
Building 31, Room 10A52
Bethesda, Maryland 20205
(301) 496-9326

THE UNIVERSITY OF ROCHESTER
MEDICAL CENTER
SCHOOL OF MEDICINE AND DENTISTRY • SCHOOL OF NURSING
STRONG MEMORIAL HOSPITAL

601 ELMWOOD AVENUE
ROCHESTER, NEW YORK 14642
AREA CODE 716

DEPARTMENT OF RADIATION BIOLOGY
AND BIOPHYSICS

December 4, 1979

TO: Members of Space Radiation Consultant Group
Federal Strategy for Research into Biological
Effects of Ionizing Radiation

FROM: George W. Casarett

RE: Outline Of Radiation Research Needs For Activities In Space.

Dear Colleagues:

Enclosed is a copy of the somewhat revised and edited Outline.

Please return to me your comments and suggestions for further change. Also, please send any suggestions you may have for "Cross Cutting Questions".

I enjoyed working with you at the meeting last week.

With best regards.

Sincerely,

George

George W. Casarett

GWC/bh

Enc.

c. Dr. O. Nygaard, NIH

Edited Version 12/3/79

G. W. Casarett

Report Of Meeting 11/29/79

Of

Space Radiation Consultant Group

To Develop Federal Strategy For Research Into The Biological Effects Of Ionizing Radiation.

Members Of Space Radiation Consultant Group

Dr. Charles M. Barnes
Dr. George W. Casarett, Chairman
Dr. Stanley B. Curtis
Col. John Pickering
Dr. Paul Rambaut
Dr. Charles Sondhaus
Dr. Epaminonda W. Stassinopoulos
Dr. Sherman Vinograd, Author for Scientific Projection Paper
Dr. Robert W. Wood

TABLE OF CONTENTS

Outline Of

RADIATION RESEARCH NEEDS FOR ACTIVITIES IN SPACE

Emphasis is placed on research needs peculiar to activities in space, especially research on high Z radiation, and unlikely to be satisfied by more conventional radiation research supported by agencies other than NASA.

I. Environmental Physics And Dosimetry

A. Definition of Radiation Environment in Space: (extra- and intravehicular).

1. Definition of Primary Environment:

a. Energetic Particles:

1). A predictive technique to relate some solar or geophysical parameter (such as solar wind speed or D_{st}) to acceleration of electrons to high energies in the solar magnetosphere. The required output consists of: spatial distribution; energy spectra; and flux intensities.

2). A model which details the evolution of the distribution (spatial, energy spectrum, flux density) of energetic electrons in the outer magnetosphere.

3). Manned applications require short term prediction of magnetic storms and substorms. Particle acceleration and plasma injection are major concerns.

4). A "disturbance model" for prediction of flux enhancements due to solar or magnetospheric activity, for a typical storm and a macrostorm.

5). Synoptic measurements of solar wind parameters to predict intermediate term (30-60 days) averages of fluxes at synchronous attitudes.

6). A model for calculation of the hardening of electron energy spectra in response to rapid diffusion caused by field-line loading.

b. Solar Flare Protons and Cosmic Rays.

1). A predictive technique which will give warning of anomalously large events (e.g., that of August 1972) hours or days in advance. Identification of precursors is the most probable method.

2). A method of accurate prediction of solar proton and HZE particle events based on solar parameters. It should give order-of-magnitude or better definition of the intensities and energy spectra. Timing is of concern.

3). A method to predict the evolution of an event from solar or interplanetary parameters, given an event on the sun.

4). Models of solar proton and HZE particle entry into the magnetosphere which include local-time and magnetic storm effects in rigidity calculations.

5). Determination of the solar parameters which correlate well with the annual integrated fluences of unattenuated interplanetary protons with various energies in the MeV range, since sunspot numbers do not.

2. Shielding Attenuation: (spacecraft, space suits, body-self).

a. 3-D analysis/evaluation of various geometries and materials.

b. Optimization of shielding materials.

c. Coordination and integration of:

1). research activities

2). compilation of data (old and new)

B. Dosimetry.

1. Identification, development, and testing of active and passive instruments for space craft differentiating between high and low LET components of incident radiation at appropriate positions.
2. Correlation and coordination of space information with ground-based systems.
3. Development and design of supporting (to active dosimeters) data reduction, interpolation, and transmission system for direct, real-time readout.
4. Development of dosimetry supporting the ground-based radiobiologic research.
5. Exploration of microdosimetric techniques for measuring radiation quality in space.
6. Study of possible unique effects of very heavy (e.g., iron) particle tracks in crystalline structures.

C. Expression of "Dose" for High LET Radiations.

Research to evolve a new and more appropriate concept or unit relating particle fluence directly to radiation risk.

II. Radiation Biology. High LET Particles

A. Animal Experimentation. (Organs, tissues, cells, in vivo or in vitro).

1. Ground-Based.

a. Review of existing, ground-based experimental data:

1) external beam data.

2) "hot particle" data.

b. Quantitative "dose"-response relationships and RBE values, in terms of conventional (rad) dose, fluence, track length, and energy, for various HZE particles, for the following early, intermediate and late biological effects. (The question of ranges of biological species should also be considered). (Influence of age and sex should also be included).

c. Effects of whole-body irradiation:

1) Life span shortening.

2) Cancerogenesis.

3) Teratogenesis.

4) Growth and development.

5) Special organ effects. Morphologic and functional (including behavioral) effects on central nervous system, and eye (retina and lens).

d. Effects of partial-body irradiation:

1) Cancerogenesis in highly susceptible organs.

2) Cataract.

3) Microlesions in central nervous system and potentially associated functional neurologic effects.

4) Microlesions in retina and potentially associated functional effects on vision.

5) Microlesions in microvasculature.

e. Cellular and molecular effects, contributing to mechanisms of HZE particle effects.

1) Cellular effects (cell kinetics, cell death versus inactivation).

2) Cell lesion enhancement.

3) Cell transformation.

4) Membrane permeability.

5) Single particle effects.

6) Functional effects on cultured non-dividing cells.

2. Aloft (in space).

a. Research Facilities

1) Strategy and cost-benefit analysis of space versus ground-based research, comparing ground-based experimentation using monotype radiation sources with research in potentially available in-space research laboratories (serviced by the Shuttle) where multi-directional, multienergetic radiations exist. Some of both may be required.

2) Design and development of prototype satellite space craft (and support requirements) dedicated to research in radiation biology and dosimetry (in conjunction with research in other life science studies).

3) Design and development of fully dedicated radiation biology satellite space craft and operational strategy.

4) Develop capability for radiation biology research in space (space craft, support facilities, trained personnel, etc.).

b. Ground-Based Preparation for Dose-Response Studies Aloft.

1) Development, selection, and placement of standard battery of flight dosimetry instrumentation.

2) Development and selection of minimal standard set of biological response end points to be examined and determined.

3) Development and selection of acceptable and sensitive tests and methods for measuring selected response endpoints.
4) Establish minimal number of advantageous experimental biological models needed for in-space research, with respect to animals (down to the subspecies level), tissue culture systems, and cell cultures.
5) Development of acceptable flight-simulation techniques for pre-flight testing of biological models and post-flight implementation of paired control studies.
6) Analyze simulated-flight data to determine possible synergistic, additive or antagonistic effects of combining radiation (of different types) with potential physiologic alterations in space, with respect to radiobiological endpoints.
7) With flight-simulation techniques, study of animal responses to well-defined radiation exposure combined with 3 (or so) levels of g.

c. Dose-Response Studies in Space, taking account of the following variables:
1) Types of radiation involved in exposure (low-LET and high-LET).
2) Dose (low, intermediate, high; single vs. fractionated).
3) Early, intermediate, and late biological effects (biochemical, in genetic material, cellular, histologic, in specific organs of special importance, and on life span of cells and animals).
4) Comparison of in-flight data with ground-based data to determine possible synergistic, additive or antagonistic effects of combining radiation (of different types) with physiologic alterations in space, for development of appropriate post-flight ground-based and future flight investigations of such effects and influences.
5) EFFECTS OF DOSE FRACTIONATION USING MULTIPLE FLIGHTS OF SELECTED ANIMAL MODEL(S).

5) Studies of animal responses to well-defined ambient radiation combined with 3 (or so) levels of g.

6) Cross-correlation of experimental and human responses as possible on a continuing basis.

B. Human Studies

1. No human radiation exposure to be conducted for purposes of experimental investigation.
2. Pre-flight, immediate post-flight, and long-term post-flight biomedical examination:
   a. Establish a carefully selected minimal battery of examination criteria (history, physical and laboratory) for pre-flight and immediate and long-term post-flight follow-up of all flight personnel.
   b. Retrospective and prospective follow-up for all potential effects of space radiation. For retrospective dose-response analysis this is heavily dependent on a standard and well-selected dosimetric system properly located aloft. This also requires a detailed report of the individual's physiological responses to flight or flights plus incident and environmental data, to rule out other possible etiological influences. Careful dosimetry and follow-up examinations required.
3. Accumulation of all other pertinent retrospective and prospective dose-response data relating to exposures to high Z or high-LET radiation exposures (e.g., radiotherapy or in accidents). Careful dosimetry and pertinent follow-up examinations required.
4. Establish dose-response data correlating facility (computerized, continuing, and probably central), for efficient communication and rapid response.

5. Biomedical research needed: (in addition to human studies indicated above and experimental research indicated in previous sections).

   1) Development of sensitive biological indicators for obtaining of data in flight by acceptable means.

   2) Development of sensitive techniques for detection and measurement of effects of space radiation exposure following flights.

   3) Development of information and techniques for determining relative susceptibility to space radiation effects among human beings, including age, sex, and other conditions.

   4) Determination of acceptable radiation exposure limits for personnel engaged in activities in space for in-space careers of various durations.

III. Operational Countermeasures

A. Body Shielding.

1. Ground-Based Research.

a. Application of current transport codes to evaluate various shielding configurations for a variety of space radiation spectra and particle mixtures.

b. Development of improved transport codes.

c. Development of organ shielding techniques.

d. Research into optimal designs for shelters.

e. Evaluation of prototype shielding concepts at accelerators that simulate space radiation.

2. Aloft.

Evaluation of prototype shielding concepts in flight.

B. Radioprotectants

1. Ground-Based Research.

a. Review of radioprotectant literature with respect to the high Z radiation (and high-LET) issue, with particular inclusion of data from the U.S.S.R.

b. Expand research to identify additional radioprotective agents.

c. Research on effectiveness of combined therapy (multiple drugs), nutritional aspects, and other areas which might provide insight into useful radioprotective measures.

d. Basic research on structural-functional relationships.

e. Research into chemicals that maintain immunity, in case of high exposure.

f. Research on benefits versus risks of radioprotectants.

2. Aloft.

   a. Drug distribution and utilization in the body at zero gravity.

   b. In-flight evaluation of radioprotectant performance. Definition of suitable endpoints is a prior requirement.

C. Amelioration.

1. Research into chemicals which may modify effects when administered post-irradiation.
2. Influence of post-irradiation physical countermeasures on radiation effect.

IV. Other Recommendations

A. Expansion of Ground-Based HZE Particle Facilities for Space-Related Research.

HZE particles constitute a relatively unexplored class of radiation, and numerous basic studies must be done to determine its characteristics and biological effectiveness at various levels of exposure and in various systems in the body.

Owing to the size and complexity of accelerators required to produce HZE particles and the current limitation of such facilities, it will be necessary not only to increase the time available for space-related research in existing facilities but also to provide additional accelerators (and support facilities) as well.

Certainly, strong endoresement should be given to continued support of the Bevilac facility at the University of California, Berkeley, and to an increase in time available for space-related research with that facility.

In addition, it is ~~strongly~~ recommended that CONSIDERATION BE GIVEN TO THE NEED FOR a new, additional, pre-dedicated HZE particle production and exposure facility ~~be~~ committed to ground-based, ~~space-related~~ research.

B. Training.

A program for training in specialized aspects of space radiation physics, biology, and protection is ~~strongly~~ recommended.

C. Radiation Protection Guidelines.

Periodic review and evaluation of space radiation protection guidelines (exposure limits), in the light of available information on effects and risks, is strongly recommended.

D. Coordination of Information.

It is necessary that all data pertinent to space radiation problems be coordinated for purposes of analysis, information retrieval, application, and research guidance. This might best be accomplished by establishment of a "space radiation data center" in which experimental and other dosimetric and biological effects data are tabulated, computerized and circulated to interested persons.

In conjunction with the above, such a data center should have translation capabilities. The USSR has collected numerous hours of experimental data on HZE particles and their effects from its space laboratories, which has not generally been made available (translated) for U.S. investigators.

Russian investigators have been hesitant to attend outside meetings to present their data. The U. S. government should attempt to host such meetings and/or assist international scientific organization in sponsoring such meetings.

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