FINAL REPORT – BRER CORE SUPPORT (DOE/ER/63977-1)
Contract provided by DOE-FG02-05ER63977 to The National Academies
Evan B. Douple, Ph.D.
Scholar, The National Academies
12/01/2004 – 11/30/2005

This contract provided core support that was used to fund the activities of The National Academies Board on Radiation Effects Research (BRER) in the Division on Earth and Life Studies. The BRER Committee consisted of 12 distinguished scientists who provided oversight and advice regarding the BRER studies in progress and provided advice regarding the development of proposals and the formation of study committees for future projects in the radiological sciences that warranted investigation. The BRER Committee included the following membership:

S. James Adelstein (Chairman), Harvard Medical School, Boston, MA
Harold L. Beck, Department of Energy Environmental Laboratory (retired), New York, NY
Joel S. Bedford, Colorado State University, Fort Collins, CO
James E. Cleaver, University of California San Francisco Cancer Center, San Francisco, CA
Sarah C. Darby, University of Oxford, Oxford, United Kingdom
Sharon L. Dunwoody, University of Wisconsin, Madison, WI
C. Clifton Ling, Memorial Sloan-Kettering Cancer Center, New York, NY
Daniel Krewski, University of Ottawa, Ottawa, Ontario, Canada
Theodore L. Phillips, University of California, San Francisco, CA
Andrew M. Sessler, E.O. Lawrence Berkeley National Laboratory, Berkeley, CA
John C. Villforth, Food and Drug Law Institute (retired), Derwood, MD
Paul L. Ziemer, Purdue University, West Lafayette, IN

During this funding period, BRER held two meetings in which the BRER committee members hosted two workshops in order to gather information in public sessions from agency officials regarding a variety of issues in the radiation sciences.

BOARD ON RADIATION EFFECTS RESEARCH

BOARD MEETING – DECEMBER 2, 2004

1:30 PM – 2:30 PM
WORKSHOP 1:
ACTIVITIES OF THE ICRP
DONALD A. COOL
Senior Advisor, Office of Nuclear Material Safety and Safeguards
U.S. Nuclear Regulatory Commission

2:30 PM – 4:30 PM
WORKSHOP 2/PANEL:
NEEDS FOR RADIATION SCIENCES IN THE ACTIVITIES OF THE FEDERAL GOVERNMENT

FOOD AND DRUG ADMINISTRATION	BRAD LEISSA — Deputy Director, Division of Counter-Terrorism, Center for Drug Evaluation and Research
	JOHN L. McCROHAN — Deputy Director, Office of Communication, Education and Radiation Programs Office of Communication, Education and Radiation Programs Center for Devices and Radiological Health
NATIONAL INSTITUTES OF HEALTH/NIAID	ERNEST TAKAFUJI — Assistant Director for Biodefense Research, NIAID
DEPARTMENT OF ENERGY	NOELLE METTING — Program Manager, Biological Effects of Radiation, Office of Science
NUCLEAR REGULATORY COMMISSION	CHERYL A. TROTTIER — Chief, Radiation Protection, Environmental Risk, and Waste Management Branch, Office of Nuclear Regulatory Research
ENVIRONMENTAL PROTECTION AGENCY	JEROME PUSKIN — Science and Risk Assessment, Radiation Protection Division, Office of Air and Radiation
NATIONAL CANCER INSTITUTE	NORMAN COLEMAN — Director, Radiation Oncology Sciences Program
DEPARTMENT OF HOMELAND SECURITY	BROOK BUDDEMEIER — Emergency Preparedness and Response Plans, Programs and Budgets, Science and Technology

BRER also used funding from this contract to support the planning, advertisement, and travel expenses for invited speakers for two Gilbert W. Beebe Symposia, one held December 2, 2004 and the second held on November 30, 2005. The programs for these two symposia follow.

THE THIRD ANNUAL GILBERT W. BEEBE SYMPOSIUM

RECENT DEVELOPMENTS IN RADIATION RISK ASSESSMENT

THURSDAY, DECEMBER 2, 2004
9:00 AM—12:30 PM

The Keck Center
The National Academies
500 5th St. NW
Room 100

Honorary Chairman, Dale L. Preston, Ph.D.
Former Chief of Statistics, Radiation Effects Research Foundation

"Cancer Incidence for the Atomic-bomb Survivors Using the New RERF Dosimetry"
Dale Preston, Ph.D., Hirosoft, Inc.

"Recent Results of Biological Studies and Their Relevance to Radiation Risk Assessment"
Robert Ullrich, Ph.D., Colorado State University

"Contributions of New Epidemiology Studies to Radiation Risk Assessment"
Ethel Gilbert, Ph.D., National Cancer Institute

The National Academies, Board on Radiation Effects Research

About Gil Beebe:

Gilbert W. Beebe died on March 3, 2003, 1 month short of his 91st birthday. Gil was renowned as a radiation epidemiologist. He conducted ground-breaking studies of mortality and morbidity among persons exposed to the atomic bombings in Japan and to the Chernobyl reactor accident in Ukraine. While at the National Academy of Sciences (NAS), Gil and others (including Michael DeBakey) had been advocating an ongoing follow-up system based on military and medical records, and it was at the NAS that Gil created the Medical Follow-up Agency to accomplish that. While at NAS, Gil worked with Seymour Jablon to organize the Atomic Bomb Casualty Commission research program to study the late effects of radiation exposure in Japanese A-bomb survivors. Later known as the Life Span Study, this remains the most important source of information on radiation-related risk of cancer and other long-term health effects in humans.

[abstracted from Ron et al., Remembrance: Dr. Gilbert Wheeler Beebe, 1912-2003, Epidemiology, Volume 14(4), July 2003, 488-489.]

Dale Preston, Ph.D., is a biostatistician and principal scientist for Hirosoft International Corporation and a consultant to the Radiation Epidemiology Branch of the National Cancer Institute. He holds a B.A. in Mathematics from California State University, Humboldt, and M.S. and Ph.D. degrees in biostatistics from the School of Public Health, University of California, Los Angeles. His current research interests include studies of radiation health effects in atomic-bomb survivors and various populations exposed to radiation as a result of the operation of the Mayak

plutonium production complex in Russia. Dr. Preston spent more than 20 years working for the National Academies at the Radiation Effects Research Foundation in Hiroshima, Japan. For most of that time he served as chief of the Department of Statistics. He spent two years as an expert scientist at the Radiation Epidemiology Branch of the National Cancer Institute. Dr. Preston has worked on numerous RERF Life Span Study reports and a number of other radiation- effect studies. He is the principal developer of the widely-used Epicure risk estimation software. Dr. Preston is a fellow of the American Statistical Association, an elevated member of the International Statistics Institute, and a member of Committee 1 of the International Commission for Radiological Protection. He has served as a consultant for UNSCEAR and the National Research Council BEIR V and BEIR VI committees.

Robert Ullrich, Ph.D., is Barbara Cox Anthony Chair in Oncology and Director of the Radiological Health Sciences and Cancer Research Program at Colorado State University. He earned his Ph.D. from the University of Rochester School of Medicine and Dentistry. He was formerly Vincent P. Collins Distinguished Professor in Radiation Oncology Research and Director of the Biology Division in the Department of Radiation Oncology at the University of Texas Medical Branch, San Antonio. Dr. Ullrich's laboratory is focused on delineating mechanisms involved in mammary tumor development after radiation exposure, the genetic control of susceptibility, and mapping the loci involved. He is a member of the National Council on Radiation Protection and Measurements and is currently President of the Radiation Research Society. He received the R.J. Michael Fry Research Award of the Radiation Research Society in 1987. Dr. Ullrich has served on the National Research Council's Panel on Space Radiation Effects, a number of National Institutes of Health advisory committees, and on the International Commission on Radiological Protection Committee 1 and the Task Group on estimates of radiation-induced cancer at low doses. He is currently a member of the National Research Council BEIR VII committee.

Ethel Gilbert, Ph.D., is a biostatistician in the Radiation Epidemiology Branch of the National Cancer Institute. She holds a B.A. in mathematics from Oberlin College and a M.P.H. and Ph.D. in biostatistics from the University of Michigan. Her current research includes studies of workers at the Mayak nuclear plant in Russia, studies of second cancers after radio- and chemotherapy, and radiation risk assessment. Formerly, Dr. Gilbert spent several years as a senior staff scientist at Pacific Northwest National Laboratories, where her research focused on epidemiologic studies of nuclear workers including combined analyses of national and international data. Dr. Gilbert is a fellow of the American Statistical Association and a member of the National Council on Radiation Protection and Measurements. She served on the National Research Council BEIR VI committee and currently is a member of BEIR VII.

THE THIRD ANNUAL GILBERT W. BEEBE SYMPOSIUM

The National Academy of Sciences, National Academy of Engineering, Institute of Medicine, and National Research Council are private, non-profit organizations which collectively comprise the National Academies. The National Academies perform an unparalleled public service by bringing together committees of experts in all areas of scientific and technological endeavor. These experts serve pro bono to address critical national issues and give advice to the federal government and the public.

www.national-academies.org

The Board on Radiation Effects Research acknowledges the generous support from the Department of Health and Human Services and the Department of Energy's Office of Science that has made this symposium possible.

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THE FOURTH ANNUAL GILBERT W. BEEBE SYMPOSIUM

RADIATION RISK ASSESSMENT: LOOKING BEYOND BEIR VII

December 5, 2005
1:00 - 5:00 pm

NAS Building
Lecture Room
2101 Constitution Ave, NW
Washington, DC

"THE UNCERTAIN WORLD OF RADIATION-RELATED RISK: POLICY IMPLICATIONS AT LOW DOSES"

BY CHARLES LAND, PH.D., BEEBE SYMPOSIUM HONORARY CHAIR

The relationship between radiation dose and cancer risk is highly quantified but also uncertain, with many identifiable and quantifiable sources of uncertainty. The dose-response relationship at very low doses is essentially unobservable, and therefore must be inferred somehow by extrapolation of observations pertaining to higher doses, adding a further layer of uncertainty. How uncertainties are perceived depends very much upon one's point of view. However, uncertainty analysis may provide a picture of radiation-related risk, as an uncertain quantity, that can serve as a common ground for discussion among interested parties with different viewpoints.

"Effects of Low Dose Chronic Exposure to Low-Let Ionizing Radiation: A 15-Country Study of Nuclear Industry Workers"
By Elisabeth Cardis, Ph.D.

A multinational retrospective cohort study of cancer mortality among nuclear industry workers in 15 countries was conducted, using a common core protocol,to provide direct estimates of cancer risk following protracted low doses of ionising radiation and to strengthen the scientific basis of radiation protection standards for environmental, occupational and medical diagnostic exposures. The first results of this study, based on 407,391 nuclear industry workers individually monitored for external radiation with a total follow-up of 5.2 million person-years are presented. Risk estimates are statistically compatible with the bases for current radiation protection standards. They range from values lower than those based on linear extrapolation from the atomic bomb survivor data, up to values that exceed this extrapolation by a factor of five for cancers other than leukaemia and by a factor of two for leukaemia. These results suggest that an excess cancer risk exists, albeit small, even at the low doses and dose-rates typically received by nuclear industry workers in this study.

"Multicellular Responses to Ionizing radiation"
By Mary Helen Barcellos-Hoff, Ph.D.

Cell function in complex three dimensional tissues is coordinated by soluble signaling peptides and by small molecules within the context of insoluble scaffolding provided by the extracellular matrix. Recent studies have highlighted crosstalk between irradiated cells and non irradiated bystander cells and have uncovered high frequency phenotypes of genomic instability in the progeny of irradiated cells that cannot be solely explained by direct radiation-induced mutation. A model of radiation response based on the systems biology principles of network interconnectivity and spatial organization of these cellular phenotypes within the higher order structure of tissues and organisms will be discussed.

"Cancer Risks at Very Low Doses: Why did the U.S. and French National Academies come to Directly Opposite Conclusions?"
by David Brenner, Ph.D.

Within the past year, both the US and French National Academies published learned reports on the cancer risks associated with low doses of ionizing radiation. The US report, BEIR-VII, concluded that "*A comprehensive review of available biological and biophysical data led the committee to conclude that the risk would continue in a linear fashion at lower doses without a threshold and that the smallest dose has the potential to cause a small increase in risk to humans.*" By contrast, the French Academy report concluded that "*At low doses and low dose rates of ionizing radiation, the pro-apoptotic effect dominates and the damaged cells, of which there are only a few, can be eliminated or controlled.*" Two very different views of the effects of very low doses of radiation. We will discuss how and why these two bodies came to such opposite conclusions, and reassess what we do and don't know about cancer risks at very low radiation doses.

For More Information:

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http://dels.nas.edu/nrsb/index.shtml

http://nationalacademies.org/

Location Details

The NAS Building
Lecture Room
2101 Constitution Ave, NW
Washington, DC 20418

About Gil Beebe: **Gilbert W. Beebe** died on March 3, 2003, 1 month short of his 91st birthday. Gil was renowned as a radiation epidemiologist. He conducted ground-breaking studies of mortality and morbidity among persons exposed to the atomic bombings in Japan and to the Chernobyl reactor accident in Ukraine. While at the National Academy of Sciences (NAS), Gil and others (including Michael DeBakey) had been advocating an ongoing

follow-up system based on military and medical records, and it was at the NAS that Gil created the Medical Follow-up Agency to accomplish that. While at NAS, Gil worked with Seymour Jablon to organize the Atomic Bomb Casualty Commission research program to study the late effects of radiation exposure in Japanese A-bomb survivors. Later known as the Life Span Study, this remains the most important source of information on radiation-related risk of cancer and other long-term health effects in humans.

[abstracted from Ron et al., Remembrance: Dr. Gilbert Wheeler Beebe, 1912-2003, Epidemiology, Volume 14(4), July 2003, 488-489.]

Charles Land, Ph.D., Honorary Chair, is a Senior Investigator in the Division of Epidemiology and Genetics, Radiation Epidemiology Branch, at the National Cancer Institute (NCI). He studied Statistics at the University of Chicago and was introduced to the epidemiology of radiation carcinogenesis during two tours with Gilbert Beebe at the Atomic Bomb Casualty Commission and the Radiation Effects Research Foundation in Hiroshima, Japan. He is a past member of Committee 1, on Risk, of the International Commission on Radiation Protection (ICRP), an Honorary Member of the National Council on Radiation Protection and Measurements, and served on the BEIR III and BEIR VII (Part I) committees. He recently chaired an NCI/CDC committee report on the use of epidemiological data for adjudicating compensation claims for cancer possibly associated with radiation exposure, and an ICRP committee report on low-dose extrapolation of estimated radiation-related cancer risk.

Elisabeth Cardis, Ph.D., currently runs the Radiation Group at the International Agency for Research on Cancer (IARC), where she was previously chief of the Unit of Radiation and Cancer and head of the Radiation Programme. She is responsible for the planning, conduct, and analyses of numerous epidemiologic studies of cancer in relation to exposure to radiation—both ionizing and nonionizing. She has been consultant to the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). She is currently a member of the Steering Committee for the EMF-Net project; of the International Advisory Committee for the WHO International EMF Project; and of the Scientific Council of the French Agence Française pour la Sécurité Sanitaire et Environnementale. She is a fellow of the Institute of Physics and is a also a member of the Scientific Council for the Joint Congress of the International Society for Environmental Epidemiology and the International Society for Exposure Assessment (ISEE-ISEA), Paris 2006. She has been responsible for numerous projects supported currently or previously under the European Commission's Quality of Life, Radiation Protection, and INCO-Copernicus Programmes.

Mary Helen Barcellos-Hoff, Ph.D., obtained an undergraduate degree in biopsychology at the University of Chicago and completed doctoral studies in experimental pathology at the University of California, San Francisco in 1986. She conducted postdoctoral research with Mina Bissell at Lawrence Berkeley National Laboratory that addressed the regulation of epithelial function by the extracelluar matrix. She joined the radiation biology program at Lawrence Berkeley National Laboratory in 1988 where she is currently a senior scientist, Chair of Cancer Biology and Deputy Director of the Life Sciences Division. Her research concerns the effects of low-dose and charged-particle radiation biology, stromal-epithelial interactions during mammary mediates carcinogenesis, and mechanisms by which TGFβ physiological and neoplastic processes in tissues.

David Brenner, Ph.D., D.Sc., is a Professor of Radiation Oncology and Public Health at Columbia University. New York. He earned an M.Sc. From St. Bartholomews' Hospital, University of London, in Radiation Physics, a Ph.D. from the University of Surrey in Physics, and has been awarded an honorary D.Sc. Degree by Oxford University. He is a radiation biophysicist focusing on mechanisms of DNA and chromosomal damage by different radiations. His research involves both designing new radiotherapy protocols and also modeling and analyzing low-dose epidemiological studies. He has served on various EPA, NAS, IAEA, and NCRP committees, including BEIR VI. He is a past recipient of the Radiation Research Society Annual Research Award and the Robert D. Moseley Annual Award from the National Council on Radiation Protection and Measurements.

Past Honorary Chairs

2002 — Gilbert W. Beebe

2003 — William J. Schull

2004 — Dale L. Preston

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Nuclear and Radiation Studies Board

Created in April 2005, the board merges the combined resources and portfolios of the Board on Radioactive Waste Management (BRWM), which was created in 1958 to advise the nation on the safe and responsible management of radioactive wastes, and the Board on Radiation Effects Research (BRER), created in 1981 to advise on the biological effects of radiation. NRSB positions the National Academies to continue the work of BRWM and BRER, and to address several new needs in nuclear and radiation science, including subjects related to terrorism and homeland security.

The Mission of NRSB

The mission of the Nuclear and Radiation Studies Board is to provide an open forum for discussion and to organize and oversee studies on safety, security, technical efficacy, and other policy and societal issues arising from the application of nuclear and radiation-based technologies, including:

- Health effects, consequences, and amelioration of exposure to ionizing and non-ionizing radiation, including periodic assessments of the biological effects of ionizing radiation.
- Generation, use, remediation, and disposition of nuclear materials and radioactive (including mixed) wastes.
- Malevolent uses of nuclear and radiation-based technologies.
- Risks, benefits, and/or efficacies of nuclear and radiation-based technologies.