Radiation Biology: A Response to the American Innovation and Competitiveness Act

A Report by the

Subcommittee on Physical Sciences
Committee on Science

of the

NATIONAL SCIENCE AND TECHNOLOGY COUNCIL

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The National Science and Technology Council (NSTC) is the principal means by which the Executive Branch coordinates science and technology policy across the diverse entities that make up the Federal research and development enterprise. A primary objective of the NSTC is to ensure science and technology policy decisions and programs are consistent with the President's stated goals. The NSTC prepares research and development strategies that are coordinated across Federal agencies aimed at accomplishing multiple national goals. The work of the NSTC is organized under committees that oversee subcommittees and working groups focused on different aspects of science and technology. More information is available at http://www.whitehouse.gov/ostp/nstc.

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About the Subcommittee on Physical Sciences

The purpose of the Physical Sciences Subcommittee (PSSC) is to advise and assist the Committee on Science and the NSTC on US policies, procedures, and plans in the physical sciences. As such, and to the extent permitted by law, the PSSC defines and coordinates Federal efforts in the physical sciences, identifies emerging opportunities, stimulates international cooperation, and fosters the development of physical sciences. It also explores ways in which the Federal government can increase the overall effectiveness and productivity of US investment in physical sciences research, especially with regard to issues that cut across agency boundaries. The PSSC also strives to enhance Federal R&D enterprise by embracing diversity, equity and inclusion, recognizing the critical importance of the participation of a broad range of backgrounds and perspectives to achieving robust science. Section 106 of the American Innovation and Competitiveness Act, Public Law 114-329 (AICA) requires the PSSC to coordinate Federal research efforts to maximize the efficiency and effectiveness of US investment in high energy physics, radiation biology, and fusion energy sciences.

About this Document

This document was developed in response to Congressional requirements in AICA regarding radiation biology. The AICA requires OSTP, through the PSSC, (A) to advise and assist on policies and initiatives in radiation biology; (B) to identify opportunities to stimulate international cooperation and leverage research and knowledge from sources outside of the US; (C) to ensure coordination between Federal departments and agencies; (D) to identify ongoing scientific challenges for understanding the long-term effects of ionizing radiation on biological systems; and (E) to formulate overall scientific goals for the future of low-dose radiation research in the US.

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Abbreviations and Acronyms

AICA	American Innovation and Competitiveness Act
ALARA	As Low As Reasonably Achievable
CANDLE	Cancer Distributed Learning Environment
CFR	Code of Federal Regulations
CIRRPC	Committee on Interagency Radiation Research and Policy Coordination
CT	Computed Tomography
DHHS	Department of Health and Human Services
DHS	Department of Homeland Security
DNA	Deoxyribonucleic acid
DOD	Department of Defense
DOE	Department of Energy
EPA	Environmental Protection Agency
FOA	Funding Opportunity Announcement
GAO	Government Accountability Office
ICRP	International Commission on Radiological Protection
LNT	Linear No-Threshold
LSS	Life Span Study
MELODI	Multidisciplinary European Low-dose Initiative
mGy	milligray
mSv	millisievert
NASA	National Aeronautics and Space Administration
NCI	National Cancer Institute
NCRP	National Council on Radiation Protection and Measurements
NIAID	National Institute of Allergy and Infectious Diseases
NIST	National Institute of Standards and Technology
NRC	Nuclear Regulatory Commission
NSF	National Science Foundation
OSHA	Occupational Safety and Health Administration
OSTP	Office of Science and Technology Policy
PSSC	Physical Sciences Subcommittee
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation

Executive Summary

The National Science and Technology Council's (NSTC's) Physical Sciences Subcommittee (PSSC), under the Committee on Science, seeks to enhance the coordination of Federal efforts related to radiation biology and maximize the efficiency and effectiveness of associated U.S. investments in response to Section 106 of the American Innovation and Competitiveness Act, Public Law 114-329 (AICA). To that end, the PSSC has the following responsibilities:

1) Advise the NSTC on policy initiatives in radiation biology;
2) Identify opportunities to stimulate international cooperation and leverage research;
3) Coordinate efforts across NIST (DOC), DOD, DOE, DHS, DHHS, OSHA (DOL), EPA, NASA, NRC, and NSF;
4) Identify scientific challenges for understanding long-term effects of ionizing radiation on biological systems; and
5) Form overall scientific goals for the future of low-dose radiation research in the United States.

The risk estimates for adverse health outcomes from low-doses and low-dose rates of radiation are uncertain which, in turn, leads to uncertainty in appropriate regulations for protection from radiation. It therefore remains critical to develop scientific approaches to reduce this uncertainty. Thus, one focus of radiation biology research is to improve radiation risk management methods and potentially establish new guidelines. In order to accomplish this, it is necessary to improve the scientific knowledge of low-dose/low-dose rate radiation effects on biological systems and develop a revised mathematical model that more accurately predicts the risks associated with low-dose radiation exposure. This new model would, for example, incorporate data generated from applying new methods for focused radiation exposures, advanced genome-enabled biological techniques, new computational approaches for analyzing large data sets, and the incorporation of more expansive epidemiological datasets. Focused domestic efforts and international cooperation in several scientific areas would be beneficial in pursuing this goal. A primary area identified for both domestic and international coordination is a shared database as a repository for radiation biology datasets that could be used by domestic agencies and international entities to identify biological mechanisms of cancer initiation, biomarkers of radiation exposure or damage, and refinement of radiation risk.

Renewed interagency coordination in the area of radiation biology will provide a needed focus. This document strongly recommends that Federal departments and agencies coordinate together, through the PSSC or a new NSTC group, to set priorities for low-dose radiation research, identify research gaps among agency programs, and help to guide research to address those gaps as well as serve as a vehicle for interagency communication of research results. This interagency group should focus on the broader issues of low-dose radiation research that fall outside, and at the margins, of existing agency missions. The coordinating group could help forge and maintain a consistent effort, and allow for communication and coordination of joint development research efforts (i.e. Funding Opportunity Announcements [FOAs]) in radiation biology. The goal for this effort would be to promote communication and research that establishes the shape of the dose-response curve for adverse health outcomes at low-doses and low-dose rates using epidemiology[1] and radiation biology data.

[1] In this context, epidemiology refers to the study of the distribution, causes, and risk factors in specified populations, and does not imply that there is a specific disease transmission vector associated with low-dose radiation.

Introduction

While few would dispute the health effects of exposure to high doses of radiation, knowledgeable experts continue to debate the potential health effects of low-dose and low-dose rate radiation. This includes the basic question of whether low doses of radiation (<100 mGy[2]) or low-dose rates (<5 mGy per hour) increase the risk of cancer in humans.[3] Radioactive materials are relatively common in the natural environment, albeit at quite low concentrations. Low-dose radiation exposure is part of everyday life, with contributions from local geology, building materials, radon gas, air travel (cosmic rays), and even consumption of certain popular fruits and vegetables. Thus, exposure to natural background levels of radiation is and always has been a pervasive fact of life on Earth. Of more recent concern is exposure to low-dose radiation with the expanding use of medical imaging technologies for medical and dental diagnoses and treatments. While these imaging technologies employ radiation doses that are still very low, they are nonetheless incrementally increasing radiation doses in exposed individuals.

Radiation at high doses is known to cause a range of cancer types in humans (radiogenic cancers). This is borne out by extensive epidemiology studies of exposed human populations [e.g. the Life Span Study (LSS) of Japanese atomic bomb survivors][4] and extensive laboratory animal model-based research. Radiation is therefore regulated as a carcinogen. However, conclusive proof of the human health risks of cancer at low doses of radiation, defined as <100 mGy, remains elusive. Because cancer is a common occurrence in human beings, detecting the independent impact of low-dose radiation is experimentally challenging. Epidemiological studies investigating links between low-dose radiation exposure and cancer in humans have shown variable and often confounded results due to the inability to separate the impact of low-dose radiation relative to other more prominent, known causes of cancer such as smoking, family history, low physical activity, alcohol use, etc.[5] In the absence of conclusive data, Federal agencies with regulatory responsibilities for protecting workers and the public from radiation exposure have relied on the linear no-threshold (LNT) dose-response model of cancer risk for radiation exposures.[6] This model is based on cancer risk estimates from populations exposed at high radiation doses (most prominently, the LSS) extrapolated to zero.

Use of the LNT dose-response model for radiation protection purposes implies that radiation exposure, however low, always carries a stochastic risk of cancer. The question has been controversial, with groups of experts arguing that low-dose radiation either a) poses a threat, b)

[2] The Gray (Gy) is a unit used to measure the amount of radiation absorbed by an object or person ("absorbed dose"). One Gy is equal to an absorbed dose of one Joule of energy per kilogram of body mass. A full body CT scan typically gives a dose of 10 mGy.

[3] "Low-dose radiation" includes low-dose and low-dose rates of radiation. Dose units expressed in mGy ≈ mSv.; National Council on Radiation Protection and Measurements. (2015). *NCRP Commentary No. 24 : Health Effects of Low-doses of Radiation: Perspectives on Integrating Radiation Biology and Epidemiology*. Bethesda, MD: NCRP.

[4] Radiation Effects Research Foundation, https://www.rerf.or.jp/en/

[5] Any analysis of the relationship between low-dose radiation and disease is complicated by the multitude of additional factors that contribute to health risk in a given population. Unambiguous extraction of a causal relation between low-dose radiation and negative health effects is exceedingly difficult.

[6] National Council on Radiation Protection and Measurements. (2001). *Report No. 136 – Evaluation of the Linear-Nonthreshold Dose-Response Model for Ionizing Radiation (2001).* Bethesda MD: NCRP.

poses no threat below some threshold level, or c) provides beneficial (hormetic) health effects.[7] A review by the National Council on Radiation Protection and Measurements (NCRP) of recent epidemiological studies concluded that, at present, continued use of the LNT dose-response model is warranted, although more recent molecular biology-based research in model systems may support alternative health effects models[8]. Despite the decades-long controversy, the LNT dose-response model, in the absence of data to validate an alternative (or better) model, remains the basis for most radiation risk analysis. National and international science advisory groups such as United Nations Scientific Committee on the Effects of Atomic Radiation, the International Commission on Radiation Protection, and the NCRP continue to recommend use of the LNT dose-response model as a basis for radiation protection.[9]

Inadequate understanding of low-dose radiation health effects, including whether or not low-dose radiation causes cancer, results in significant societal and financial impacts. If, as the LNT dose-response model implies, there is no “safe” dose of radiation, then some will argue that all radiation exposure must be completely avoided at all costs, an impossible prospect but one that has led some to reject medical and dental procedures. Current regulations governing many aspects of radiation safety including nuclear plant and medical facility construction, nuclear waste storage, remediation targets, and worker/patient protection programs follow an ALARA (As Low As Reasonably Achievable) based dose limit approach to safeguard against unnecessary radiation exposure.

This broad regulatory practice, based ultimately on the LNT dose-response model, seeks to limit radiation exposure to as low as reasonably achievable (taking into account economic and social well-being), sometimes imposing controls well below natural background radiation levels. If, as some experts believe, a threshold level for low-dose exposure could be demonstrated, it may be possible to revise regulatory guidance in ways that would provide significant cost savings by reducing compliance costs while mitigating risks. Resolving scientific uncertainties of the health impacts of low-dose radiation could also alleviate fears among some members of the public on the associated environmental, occupational, or sociological impacts, although this may be a significant challenge.

Recent reports on low-dose and low-dose rate radiation research in the United States have documented a decline in Federal funding, but also the need for closer collaboration among current and future research programs and international efforts.[10] Many Federal agencies conduct or fund research in this area according to their agency’s mission and budgeting priorities. Others conduct activities where a better understanding of the health effects of low-dose radiation is relevant (Figure 1).

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[7] Mossman, K. (2001). Deconstructing Radiation Hormesis. *Health Physics*, 80:(3) 263-269.; Feinendegen, L., & Cuttler, J. (2018). Biological Effects From Low-doses and Dose Rates of Ionizing Radiation: Science in the Service of Protecting Humans, A Synopsis. *Health Physics*, 114(6) 623-626.

[8] National Council on Radiation Protection and Measurements. (2018). *Commentary No. 27 – Implications of Recent Epidemiologic Studies for the Linear-Nonthreshold Model and Radiation Protection (2018).* Bethesda, MD: NCRP.; Paunesku, *et al.* (2017). Biological basis of radiation protection needs rejuvenation. *International Journal of Radiation Biology*, 93:(10) 1056-1063.

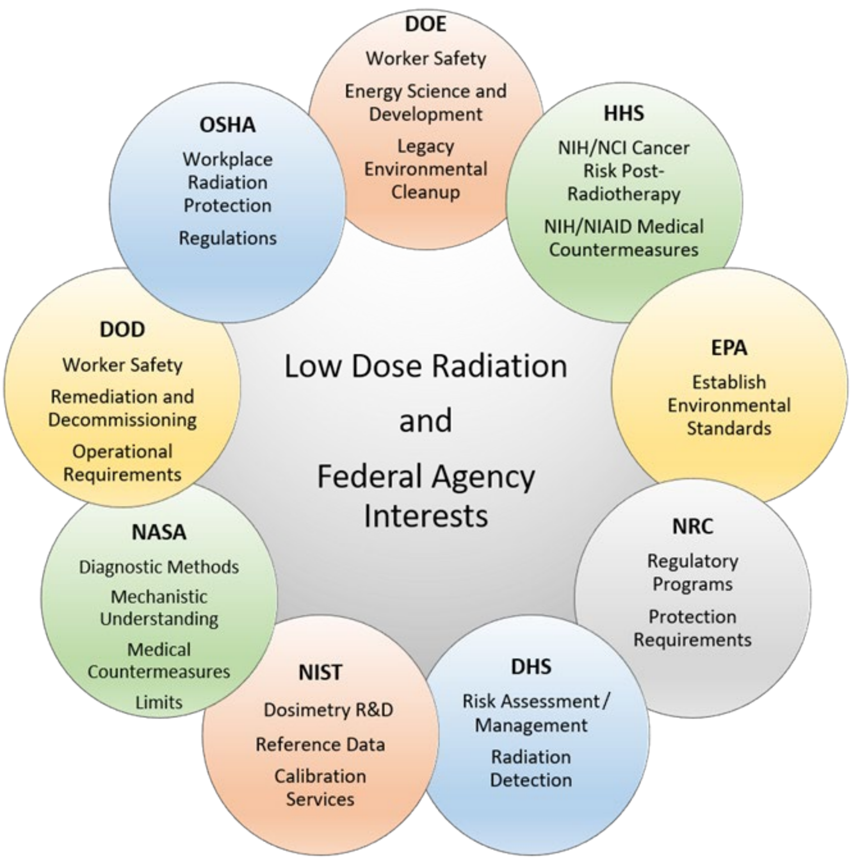
[9] United Nations Scientific Committee on the Effects of Atomic Radiation. (2012). *Biological Mechanisms of Radiation Actions at Low-doses.* New York, NY: United Nations. ; ICRP. (2005). ICRP Publication 99 Low-dose Extrapolation of Radiation-related Cancer Risk. *Annals of the ICRP*, 35(4).

[10] United States Government Accountability Office. (2017). *Low-dose Radiation - Interagency Collaboration on Planning Research Could Improve Information on Health Effects.* Washington, DC: United States Government Accountability Office.

In light of the importance of defining the health effects of radiation at low doses, this report identifies opportunities for international cooperation and leveraging of research findings, recommends actions to ensure coordination among US agencies with a regulatory role or an interest in this area, identifies ongoing scientific challenges, and formulates scientific goals for low-dose radiation research.

Federal Agency Stakeholders

Many agencies within the Federal government conduct activities for which a clearer understanding of the health effects of low-dose radiation would be beneficial. Several agencies are directly involved in radiation protection regulation, others are directly involved in human health research, and still others are responsible for operations under a variety of radiation threat scenarios (Figure 1).



Scientific Challenges and Opportunities

Much is known about radiation effects (at medium and high doses) on human health. This knowledge stems from extensive medical and epidemiological studies of human populations exposed to radiation. The LSS of atomic bomb survivors from Japan is one of the most complete of these larger scale studies. This cohort has been extensively monitored for decades for health-associated effects (cancer and non-cancer) that can be ascribed to varying levels of radiation exposure. Much of the epidemiologic data at medium to high total-body doses (1-4 Gy) is derived from the LSS, which provides a data- and science-informed estimate of cancer risk for a given dose of radiation. Many of the radiation protection regulations developed in this country and internationally are based in part on the findings of the LSS. However, the LSS data set does have limitations: Most of the data in the study are for acute doses of radiation as opposed to those normally, or occupationally experienced by the public.

To estimate the human health risks of cancer at low-doses (<100 mSv[11]), regression of the epidemiological data must be made to much lower dose levels, namely those outside the range where there is extensive data coverage and where reliable data for radiation-induced cancers are unlikely given their low frequency in the context of the high background frequency of cancers in humans. This extrapolation can assume many mathematical forms, but, with significant uncertainty associated with health effects data in the low-dose range, national and international bodies have to date accepted the LNT dose response model's linear extrapolation from radiation epidemiology data (including data from the LSS study) through zero as the best available model of low-dose radiation risk[12]. In the absence of clear data to indicate otherwise, the LNT dose-response model assumes that the risk of cancer is a linear function of radiation dose.

For decades, the LNT dose-response model has continued to be debated in the scientific literature. This is partly due to the scientific and technological difficulty in conducting research at doses below 100 mSv. Purely epidemiological studies targeting the low-dose region have been difficult and costly primarily because of the significant challenges in assembling suitably large cohorts of individuals with a known range of radiation exposure and associated health and medical data. These studies typically require at least hundreds of thousands of subjects in order to have enough statistical power to formulate conclusive results. Cohorts to date have been compromised radiation workers, medical patients/technicians, or industrial workers, situations in which radiation doses are known or can be reconstructed along with health records or mortality outcomes. More recent studies have included nuclear industry workers and large cohorts of pediatric patients who received CT scans[13]. The challenge in all these studies is detecting cancer incidences that can be attributed solely to low-dose radiation as opposed to those cancers resulting from more prevalent causes (e.g. smoking, alcohol use, diet, lack of physical activity). Even the best designed epidemiological

[11] The Sievert (Sv) is a unit used to describe the biological effect of a radiation dose ("equivalent dose"), and is equal to the absorbed dose in Gy multiplied by a factor that represents how biological effects respond to different types of radiation. For a typical CT scan, the equivalent dose measured in Sv is equal to the absorbed dose in Gy

[12] Brenner, *et al*. (2003). Cancer risks attributable to low-doses of ionizing radiation: Assessing what we really know. *PNAS*, 100 (24) : 13761–13766.

[13] Leuraud, *et al*. (2015). Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS): an international cohort study. *Lancet Haematol*, 2: e276–81. ; Richardson, *et al*. (2015). Risk of cancer from exposure to ionizing radiation: a retrospective cohort study of workers in France, the United Kingdom, and the United States (INWORKS). *BMJ*, 351:h5359. ; Meulepas, *et al*. (2019). Radiation Exposure From Pediatric CT Scans and Subsequent Cancer Risk in the Netherlands. *The Journal of the National Cancer Institute*, 111:(3) 256-263.

studies examining low-dose radiation exposure in humans will be subject to some debate because they are observational rather than controlled experiments. More recent data collection and record keeping efforts may produce more controlled studies and provide a much more accurate estimate of low-dose risk by addressing traditional confounding factors such as smoking and non-radiation-induced cancers, but these studies are either in progress or yet to come (discussed below).

Future Research Opportunities

Recent significant advances in cellular technologies and computational analysis have significantly increased understanding of the underlying mechanisms of cancer and non-cancer disease formation by assessing changes at the genome, gene expression, and protein levels. Incorporating such mechanistic information in the development of some form of biologically based dose-response model will be critical to better estimation of low-dose and low-dose rate adverse health effects. Proposed approaches have been discussed in various venues including a subcommittee of DOE's Biological and Environmental Research Advisory Committee;[14] a recent workshop supported by the American Nuclear Society's Eastern Washington section;[15] a May 2019 discussion at the National Academies Beebe Symposium; and in publications from NCRP and others.[16] Some of these new avenues for research are also discussed below.

Big Data Epidemiology

Some have suggested that the introduction of high-performance computing techniques and enhanced data collection into many areas of science offer opportunities for improved epidemiological studies. Efforts such as the Million Veterans Program, the *All of Us* program, the Million Person Study, as well as new methods to assemble and integrate medical records to help guide medical treatments for cancer,[17] have shown some promise in offering ways to examine very large disparate datasets in new ways. More than just novel computational capabilities, the collection and assembly of ever broader health and medical data affords new opportunities to more directly address confounding issues in epidemiological studies. For example, detailed health records could allow better reconstructions of radiation exposure from medical and dental imaging techniques, often a source of uncertainty in epidemiological studies. Changes in data collection, integration, and analyses brought on by developments in information technology may provide opportunities to assemble robust, multifaceted datasets not possible in previous decades, with potential applications to low-dose radiation research. As there is no current evidence that large data sets will suffice to improve understanding, it will be important to do rigorous research to understand whether such large data sets can meaningfully address confounding issues in epidemiology around low-dose exposures and low-frequency events. Such large epidemiological studies will still have to overcome the influence of background cancer levels in order to measure the low frequencies of radiation-induced cancers. Any discovery of radiation-specific markers of cancer and non-cancer diseases could of course greatly mitigate this challenge.

Enhanced Model Systems

Enhanced model systems might be employed in the conduct of a low-dose research program to improve the estimates of risk. Ethical concerns appropriately preclude direct experimentation on humans, but new model systems could be explored for low-dose radiation research to better translate experimental results to human health impacts and bridge laboratory observations with

[14] Low-dose Letter and BERAC Report 2016

[15] https://www.anseasternwashington.org/lowdose-2018.html

[16] National Academies of Sciences, Engineering, and Medicine. (2019). *The Future of Low-dose Radiation Research in the United States: Proceedings of a Symposium.* Washington, DC: The National Academies Press. https://doi.org/10.17226/25578.

[17] Million Veterans Program, https://www.research.va.gov/mvp/; *All of Us,* https://allofus.nih.gov/; Boice, *et al*. (2018). The Past Informs the Future : An Overview of the Million Worker Study and the Mallinckrodt Chemical Works Cohort. *Health Physics*, 144(4): 381-385.; CANcer Distributed Learning Environment (CANDLE), https://candle.cels.anl.gov/.

epidemiological studies. Early medium and low-dose research using laboratory animals focused on model experimental systems such as dogs and mice.[18] In recent years, a number of animal models have been developed that may provide reliable extrapolation to radiation response in humans, including at low-doses. For example, there are genetically-modified mice that have mutations in cancer-specific genes making them uniquely sensitive to cancer induction by a number of agents, including radiation.[19] The incorporation of mutations that result in radiation-sensitivity can enhance the utility of such mouse models for investigating the induction of cancers by radiation and make available specific radiation-induced cancers for molecular characterization. The so-called humanized mouse models, which involve human tissues and organs transplanted into mice,[20] offer additional model systems that may be more predictive of human outcomes.

Bioindicators/Biomarkers for Low-dose/Low-dose Rate Radiation

When considering the use of mechanistic data in the enhancement of low-dose risk assessment, it is informative to distinguish between cellular/molecular alterations directly involved in the induction of cancer and general cellular alterations that are simply a response to radiation or other stressors that could influence the likelihood of inducing cancer. For mechanistically-based predictive models of adverse health outcomes, such bioindicators will be the most informative and serve as model parameters. Most radiation-induced responses at low doses (and medium/high doses) that have been described to date are for biomarkers. For example, specific markers for double-strand DNA breaks (repair mechanisms), gene expression changes, and shifts in metabolic function have been observed for cells exposed to low-dose radiation. Certain repair mechanisms have been shown to be specifically attributable to low-dose radiation and demonstrably different from repair mechanisms stimulated at high doses[21]. Researchers should seek further to identify and quantify bioindicators for cancer (and non-cancer disease where possible). Given such bioindicators, experiments could relate total exposure and exposure rates to specific processes occurring in cells[22]. This is an exceedingly difficult challenge, but essential to building a scientific understanding that reconciles epidemiological and radiobiology results. Given the new developments discussed above in "big data" science and computation, new/improved model systems, and new bioindicator/biomarker development, it may be possible to scientifically bridge a gap between epidemiology (i.e., the data analysis from human population) and experimental science (i.e., laboratory-based) for low-dose research. The epidemiological analyses of large and enhanced datasets currently under development could help reduce health risk uncertainties in the low-dose range, whereas experimental research with model laboratory animal and cellular systems could identify and utilize new specific biomarkers and bioindicators for both radiation exposure and cancer initiation. Ideally, these new efforts would converge such that cellular processes from

[18] Brooks, A. (2018). *Low-dose Radiation : A History of the U.S. Department of Energy Research Program.* Pullman, WA: Washington State University Press.

[19] Castle, *et al*. (2017). Genetically engineered mouse models for studying radiation biology. *Translational Cancer Research*, 6(Suppl 5):S900-S913.

[20] Holzapfel, *et al*. (2015). Concise review: Humanized models of tumor immunology in the 21st century: Convergence of cancer research and tissue engineering. *Stem Cells*, 33(6): 1696-1704.

[21] Lall, *et al*. (2014). Low-dose radiation exposure induces a HIF-1-mediated adaptive and protective metabolic response. *Cell Death and Differentiation*, 1–9.

[22] Preston, R.J. (2017). Can radiation research impact the estimation of risk? *International Journal of Radiation Biology*, 93:10, 1009-1014.

new experimental results would at least partially explain new health risk observations from epidemiological studies (as proposed by NCRP[23]).

Improved Risk Model for Low-Dose Radiation

The ultimate goal of a low-dose radiation research program is to establish a mathematical model that can accurately predict risks at low-doses and low-dose rates. Such a model would incorporate knowledge derived from radiation biology and additional modifying factors (e.g. dose rate effects, radiation quality effects, genomic instability, genetic effects) to both predict epidemiological results over the observable range and extend epidemiological results outside the observable range. In addition, such a model would be predictive of risks in multiple settings. There are several biologically-based dose-response model approaches described in the literature for which improvement in predictive value can be enhanced by incorporating more informed mechanistically-based parameters. Future research should work toward integrating radiobiology and epidemiology in a systems biology approach that predicts biological response both within the range of background radiation conditions, and under somewhat enhanced radiation conditions.

[23] National Council on Radiation Protection and Measurements. (2015). *NCRP Commentary No. 24 : Health Effects of Low-doses of Radiation: Perspectives on Integrating Radiation Biology and Epidemiology.* Bethesda, MD: NCRP.

Interagency Collaboration Opportunities and Recommendations

Currently, several agencies are involved either directly or tangentially in low-dose radiation research or have a need to better understand the risks posed by low-dose radiation (Fig. 1 and Appendix). Coordination and communication among stakeholder agencies are advantageous both to communicate developments in the science and in the application and implementation of new research findings. A mechanism for continued communication can also serve as a vehicle to stimulate more active coordination where agencies have mutual interest and the flexibility to do so. For example, DOE and NASA have previously issued joint Funding Opportunity Announcements (FOAs) in low-dose radiation research, and there are other demonstrated examples of interagency coordination in the field of radiation biology.[24] Going forward, stakeholder agencies could find additional opportunities for partnerships.

As another example, the Committee on Interagency Radiation Research and Policy Coordination (CIRRPC) was charged with coordinating radiation research and policy among Federal agencies and evaluating and coordinating Federal efforts on designated radiation research projects. CIRRPC was chartered in 1984 by the Science Advisor to the President and OSTP Director. OSTP was concerned with ensuring that regulations to control radiation exposures in the workplace, and especially levels of radioactive materials in the environment, were based on the best available and credible scientific evidence. CIRRPC consisted of a policy committee and a science panel. The policy committee, which included sub-cabinet level and senior policy level representatives, identified and set priorities for, and sought resolution of, Federal radiation research and exposure issues upon request from the OSTP Director and Federal agencies. The science panel consisted of senior radiation scientists from the member agencies. CIRRPC acted as a coordinator, clearinghouse, and evaluator of Federal radiation research. It coordinated radiation policy among agencies, resolved policy conflicts, and advised on the formulation of broad radiation research policy. The CIRRPC provides a historical perspective on how to coordinate Federal radiation protection regulations based on the best available science that can be applied in the present-day context.

[24] Young, A., & Dix, G. (1988). The Federal Approach to Radiation Issues : The Committee on Interagency Radiation Research and Policy Coordination addresses these Issues. *Environ. Sci. Technol.*, 22(7) 733-739

Recommendation: Low-dose Radiation Interagency Coordination Group

NSTC should leverage PSSC or establish another interagency group to coordinate low-dose radiation research among relevant Federal agencies and with international partners. Member agencies should include NIST (DOC), DOD, DOE, DHS, DHHS, OSHA (DOL), EPA, NASA, NRC, NSF. The primary goal of this group would be to promote communication and a course of research that reduces uncertainty in risk estimates for adverse health outcomes (cancer and non-cancer) and establishes the shape of the dose-response curve for adverse health outcomes at low-doses and low-dose rates of ionizing radiation.

The low-dose radiation interagency coordination group should include the following within its scope of activities:

- ***Prioritize defining the threshold of impact for low-dose / low-dose rate.***
- ***Perform research progress reviews and portfolio gap analyses.***
- ***Investigate the creation of a web-based collaboration platform/portal for reproducible analyses, data, and research report sharing.***
- ***Host an annual research forum to discuss on-going research.***
- ***Update research priorities for federally funded low-dose research periodically.***
- ***Address competing priorities and redundancies in research to improve efficiency of effort.***
- ***Coordinate with national and international stakeholders.***
- ***Encourage alignment of radiation protection regulations with up to date radiation biology findings and recommendations.***
- ***Collaborate on best practices for implementation due to any changes in regulations.***
- ***Innovate to build leadership teams and a workforce that reflects the diversity of America in terms of gender, race, ethnicity, geography, and other characteristics.***
- ***Promote education and training opportunities that are equitable and inclusive in cultivating the next generation of radiation biologists, epidemiologists, statisticians and physicists.***
- ***Strategize and implement creative measures to counter misinformation and disinformation about radiation science.***

Conclusion

Low-dose radiation research touches on the missions of many agencies within the Federal government. These missions will benefit substantially from better coordination and communication of research findings within the broader Federal community as well as internationally. Research that reduces current uncertainties in the health risks posed by low-dose radiation can have huge implications for radiation-protection policies worldwide. Establishing a new interagency coordination mechanism will improve the Federal government's ability to leverage new scientific and technological developments and approaches related to radiation biology, share information, better advise on and plan Federally supported low-dose radiation research, and inform potential improvements to radiation protection regulations.

Appendix – Agency Mission Descriptions

Agency	*Mission*	*Low-dose Radiation Relevance*
NIST (DOC)	Promote US innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve our quality of life.	The NIST Radiation Physics Division maintains and disseminates the national measurement standards for ionizing radiation and radioactivity, conducts dosimetry research and development (R&D), and provides reference data and calibration services to stakeholders in government and industry. NIST also produces reference materials and reference methods. Metrology provided by NIST plays an important role in establishing ground-truth values and measurement traceability, which will be important for research into biological effects of low-dose ionizing radiation where the effects are likely small, with low signal-to-noise. Large multiple-institute studies spanning long periods of time will require precise measurements to reveal small effects, and trusted measurement standards to harmonize results among institutes and across time.
DoD	Provide the military forces needed to deter war and to protect the security of our country. Conduct of this mission requires readiness to operate in environments that could expose personnel to low-doses of ionizing radiation.	DoD medical research in support of this mission is guided by three strategic goals: Better Prepared, Better Protected, and Better Cared For. Understanding, preventing, and mitigating the adverse health effects of low-doses of ionizing radiation bears a relationship to each of these goals. The unifying principle is the reduction or ideally the elimination of these deleterious health effects within the context of the DoD's mission to accomplish the nation's security objectives. The research strategy is executed by: (1) driving innovation in medical R&D, (2) maintaining strong medical R&D partnerships and leveraging synergies with other government agencies, industry, and academia, (3) coordinating and integrating medical R&D portfolios across DoD, and (4) further optimizing resource management and efficiencies. These research efforts are currently distributed across multiple DoD components. The end-state vision for DoD medical research related to low-doses of ionizing radiation includes: (a) diagnostic methods and devices to rapidly and accurately identify casualties in need of immediate, delayed, and chronic medical care; (b) detailed mechanistic understanding of radiation injury to promote faster development of, and the Food and Drug Administration's approval of, new products; and (c) pharmaceutical intervention to prevent delayed or chronic injury from radiation exposure (e.g., leukemia) to reduce long-term military medical care expense.

DOE	Ensure US security and prosperity by addressing its energy, environmental and nuclear challenges through transformative science and technology solutions.	The overall DOE mission spans four major areas of emphasis: 1) Energy - Catalyze the timely, material, and efficient transformation of the nation's energy system and secure US leadership in energy technologies; 2) Science and Innovation - Maintain a vibrant US effort in science and engineering as a cornerstone of our economic prosperity with clear leadership in strategic areas; 3) Nuclear Safety and Security - Enhance nuclear security through defense, nonproliferation, and environmental efforts; and 4) Management and Operational Excellence - Establish an operational and adaptable framework that combines the best wisdom of all Department stakeholders to maximize mission success. Several Offices within DOE have an interest in low-dose radiation health effects, including: • The Office of Health and Safety establishes worker safety and health requirements and expectations for the Department to ensure protection of workers from the hazards associated with Department operations. The Office conducts health studies to determine worker and public health effects from exposure to hazardous materials associated with Department operations and supports international health studies and programs. • The Office of Environmental Management works to address the Nation's Cold War environmental legacy resulting from five decades of nuclear weapons production and government-sponsored nuclear energy research. • The Office of Nuclear Energy works to advance nuclear power to meet the Nation's energy, environmental, and national security needs.
DHS	Oversee domestic security, while facilitating lawful customs and exchange.	Components of DHS include Customs and Immigration Service, Immigration and Customs Enforcement, Customs and Border Protection, Federal Emergency Management Agency, US Secret Service, Transportation Security Agency, and the US Coast Guard. The component personnel have varying levels of exposure to and use of radioactive materials and radiation producing devices during the course of executing their diverse duties and responsibilities. Other offices, such as Science and Technology, Countering Weapons of Mass Destruction, and Safety and Health also have duties and responsibilities that are concerned with exposure to and use of radioactive materials and radiation producing devices.

		DHS interest in low-dose radiation research is predominantly focused on applied research as it relates to decision-making and risk assessment/management during and following an incident involving radiation and/or radioactive materials. Related areas of interest are radiation detection in the low-dose/dose rate regime and risk communication related to low-dose/dose rate exposures. The DHS offices that have responsibility for this area are the Countering Weapons of Mass Destruction (CWMD) Office and the Science and Technology Directorate, under which the National Urban Security Technology Laboratory resides.
DHHS	Enhance the health and well-being of all Americans, by providing for effective health and human services and by fostering sound, sustained advances in the sciences underlying medicine, public health, and social services.	Radiation Research Program (RRP), in the NCI Division of Cancer Treatment and Diagnosis (DCTD), is responsible for clinically-related extramural radiation research program. Radiation Epidemiology Branch (REB), in the NCI Division of Cancer Epidemiology and Genetics (DCEG). The research mission of the REB is to identify, understand, and quantify the risk of cancer in populations exposed to medical, occupational, or environmental radiation, and to advance understanding of radiation carcinogenesis. Radiation and Nuclear Countermeasures Program, within the National Institute of Allergy and Infectious Diseases (NIAID). NIAID is the lead Institute within NIH for the development of medical countermeasures to mitigate/treat radiation injuries.
OSHA (DOL)	Ensure safe and healthful working conditions for workers by setting and enforcing standards and by providing training, outreach, education and assistance.	OSHA standards cover employee exposures to ionizing radiation from sources not regulated by NRC or other Federal agencies; examples include x-ray equipment, electron microscopes and naturally occurring radioactive materials. Under OSHA's Ionizing Radiation standard (29 CFR 1910.1096), employers must, among other things, ensure that occupational dose limits are not exceeded; survey radiation hazards; supply appropriate personnel monitoring (e.g., dosimeters); post caution signs, labels, and signals; provide instruction to personnel; and post operating procedures. OSHA standards also cover emergency responders and other workers who may be exposed to radiological materials during an emergency or clean-up activities (29 CFR 1920.120). More information on OSHA standards is available at: https://www.osha.gov/SLTC/radiationionizing/.

EPA	Protect human health and the environment.	EPA sets generally applicable nuclear fuel cycle standards under the Atomic Energy Act (AEA) for controlling radioactivity in the environment (offsite air, water and soil) that are enforced by the NRC or its delegated Agreement States. EPA sets radionuclide-in-drinking-water limits (MCLs) under the Safe Drinking Water Act (SDWA) and determines clean up levels for radioactively contaminated Superfund sites under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Certain radionuclide air emissions are regulated under the Clean Air Act. EPA has various other authorities for controlling radioactive waste management and resulting public doses. Under the Federal Guidance authority, EPA's role is to "...advise the President on radiation matters, directly or indirectly affecting the public, including [nonbinding] guidance for all federal agencies in the formulation of radiation standards..."
NASA	Lead an innovative and sustainable program of exploration with commercial and international partners to enable human expansion across the solar system and bring new knowledge and opportunities back to earth. Support growth of the nation's economy in space and aeronautics, increase understanding of the universe and our place in it, work with industry to improve America's aerospace technologies, and advance American leadership.	The NASA Human Research Program Space Radiation Element is currently focusing on radiation research to understand the radiation risks associated with longer duration missions which have doses and rates much higher than those in the LNT dose-response model range. The primary responsibility of the Space Radiation Element is to develop predictive models for adverse outcomes from long duration, space radiation exposure. The Human Factors and Behavioral Performance Element studies the area of radiation induced health effects on the central nervous system and the combined effects associated with spaceflight that may adversely impact an astronaut or mission. NASA's Space Life and Physical Sciences Research Applications Division provides fundamental research that leads to selection of countermeasures that may be effective in spaceflight when combining microgravity along with radiation and other spaceflight stressors. NASA's radiation research performed by all of these groups helps determine and set the permissible exposure limits for astronauts. The NASA Space Radiation Analysis Group is responsible for ensuring astronauts do not exceed the permissible exposure limits during missions.

NRC	License and regulate the Nation's civilian use of radioactive materials to provide reasonable assurance of adequate protection of public health and safety and to promote the common defense and security and to protect the environment. NRC's regulatory mission covers three main areas: • Reactors – Commercial reactors for generating electric power and research and test reactors used for research, testing, and training • Materials – Uses of nuclear materials in medical, industrial, and academic settings and facilities that produce nuclear fuel • Waste – Transportation, storage, and disposal of nuclear materials and waste, and decommissioning of nuclear facilities from service	Low-dose radiation research has significant potential impact on NRC's regulatory programs through any changes to the system of radiation protection, which is generally subscribed to globally in regulatory agencies (i.e., justification, dose limits, and ALARA). A more complete understanding of the low-dose health effects of radiation would reduce uncertainty to regulatory agencies charged with protecting workers and the general population from radiation exposure. Regulatory agencies could then potentially modify their regulatory programs to better ensure protection requirements are commensurate with risks. Additional clarity on the exact nature of low-dose radiation health effects could help in removing the uncertainty in the predictive ability of radiation induced cancer risk assessments. Toward that end, the more accurate the risk assessment, the more certain the correct regulatory action can be established to mitigate the risk.