

TRANSITIONING FROM HIGH-ACTIVITY RADIOACTIVE SOURCES TO NON-RADIOISOTOPIC (ALTERNATIVE) TECHNOLOGIES

A Best Practices Guide for Federal Agencies

PRODUCT OF THE
INTERAGENCY WORKING GROUP ON
ALTERNATIVES TO HIGH-ACTIVITY RADIOACTIVE
SOURCES,
SUBCOMMITTEE ON NUCLEAR DEFENSE
RESEARCH AND DEVELOPMENT,
COMMITTEE ON HOMELAND AND NATIONAL SECURITY
OF THE NATIONAL SCIENCE AND TECHNOLOGY COUNCIL



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EXECUTIVE OFFICE OF THE PRESIDENT
NATIONAL SCIENCE AND TECHNOLOGY COUNCIL
WASHINGTON, D.C. 20502

Dear Colleagues:

High-activity radioactive sources are commonly used in medical, research, and industrial applications in the United States and worldwide. These sources present a security concern due to their potential use in radiological dispersal devices (dirty bombs) or radiological exposure devices. Although there has not been an event in the United States involving intentional malicious use of a high-activity radioactive source, the U.S. Government is considering steps that can be taken to minimize the security risks associated with radioactive sources. Non-radioisotopic alternatives to high-activity radioactive sources have emerged in recent decades, demonstrating marked improvement in reliability, operability, viability, and availability. In certain cases, non-radioisotopic alternatives offer a means for permanently reducing risk and for reducing cost.

This Administration has been a strong champion of initiatives to minimize nuclear and radioactive materials. In the U.S. National Progress Report to the 2016 Nuclear Security Summit, the United States highlighted “minimizing nuclear and other radioactive materials” as a key focus area in strengthening nuclear security implementation, and stated: “The United States will continue to develop initiatives for reducing the number of vulnerable high activity radioactive sources through continued research and development on non-radioisotopic alternative technologies, international workshops and collaboration, and direct site engagement.”

I am pleased to release this report identifying recommendations for the Federal government to transition to alternative non-radioisotopic technologies. Federal agencies involved in the procurement, use, funding, operation, certification, and licensing, and certification of high-activity radioactive sources participated in the development of this Best Practices Guide, examining existing policies, practices, and efforts affecting the transition to alternative technologies, soliciting inputs from external stakeholders.

Sincerely,



Steve Fetter
Principal Assistant Director
National Security and International Affairs
Office of Science and Technology Policy

December 2, 2016

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About the Interagency Working Group on Alternatives to High-Activity Radioactive Sources

The Interagency Working Group on Alternatives to High-Activity Radioactive Sources (GARS) was chartered on June 8, 2015, by the NSTC Committee on Homeland and National Security, Subcommittee on Nuclear Defense Research and Development. In accordance with its charter, GARS developed this guide. The charter for GARS called for an assessment of Federal agency involvement with high-activity radioactive sources and development of best practices on how agencies can incorporate the transition to alternative technologies into their strategic plans.

About this Document

GARS members developed this document to provide background information and recommendations to Federal departments and agencies on best practices for transition from high-activity radioactive sources to, or novel adoption of, non-radioisotopic technologies in cases where they meet technical, operational, and cost requirements for the end users. This document is a product of 12 months of meetings, presentations, deliberations, and discussion by GARS members as well as a half-day external stakeholder workshop. OSTP published the document.

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**NATIONAL SCIENCE AND TECHNOLOGY COUNCIL
COMMITTEE ON HOMELAND AND NATIONAL SECURITY
SUBCOMMITTEE ON NUCLEAR DEFENSE RESEARCH AND DEVELOPMENT
INTERAGENCY WORKING GROUP ON
ALTERNATIVES TO HIGH-ACTIVITY RADIOACTIVE SOURCES**

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Executive Summary

Radioactive sources commonly used in medical, research, and industrial applications in the United States and elsewhere pose a security concern due to their potential for use in radiological dispersal devices (dirty bombs) or radiological exposure devices. The U.S. Government is considering how to reduce this security risk by adopting non-radioisotopic alternatives. Though existing radioactive technologies have a proven record of reliability and effectiveness, some non-radioisotopic alternatives that have emerged in recent decades demonstrate marked improvement in reliability, operability, viability, and availability. In certain cases, these alternatives offer a means for permanently reducing risk and cost by minimizing storage and final disposition charges.

In accordance with its charter, the Interagency Working Group on Alternatives to High-Activity Radioactive Sources (GARS) developed this guide to provide Federal departments and agencies with background information and recommendations on best practices for transitioning to non-radioisotopic technologies in cases where those technologies meet users' technical, operational, and cost requirements. The guide focuses on transitioning to non-radioisotopic technologies in medical applications, but many of these best practices could be broadly applicable to other uses of high-activity radioactive sources.

In developing the guide, GARS assessed the state of research and development on non-radioisotopic technologies and compared these technologies' costs and capabilities with those of relevant radioactive sources used in comparable applications. GARS also reviewed Federal practices, policies, and regulations that affect the use of high-activity radioactive sources and their alternatives and explored ways to support the long-term transition to non-radioisotopic technologies. GARS also examined ways for the Federal government to lead by example and to enhance U.S. competency in developing sustainable and effective alternative technologies and facilitating their commercialization, availability, and use.

GARS identified recommendations that span the range of possible Federal actions in four categories: (1) Federal Procurement or Grant-Making; (2) Agency Priorities; (3) Education and Outreach; and (4) Research and Development. The recommendations may not be applicable to or feasible for all departments and agencies, but they represent potential best practices for Federal agencies considering a transition to or new adoption of alternative technology. In addition, the working group drew the following five conclusions from this effort:

- Federal departments and agencies should promote adoption of alternative technologies in federally funded programs and facilities by encouraging voluntary incentives, dedicated funding, and facilitated conversion.
- Federal departments and agencies should involve all key stakeholders in adoption of alternative non-radioisotopic technologies in the transition and should recognize the role of manufacturers, distributors, and others in developing a sustainable system for managing radioactive devices.
- When comparing technologies, Federal departments and agencies should consider the full life-cycle costs of high-activity radioactive sealed sources, including costs of security, disposition, and potential liability.
- Federal departments and agencies pursuing alternative technology replacements must balance the respective operational and technical needs of the user communities and device stakeholders with national security.

- Users, in compliance with Federal safety and physical security requirements for use of category 1 and 2 radioactive sealed sources in medical applications are likely to continue using these sources for a considerable time, especially if non-radioisotopic alternatives are not suitable for their purposes.

The recommendations presented in this guide identify opportunities for Federal departments and agencies to take steps that will facilitate the transition to non-radioisotopic technologies where appropriate. Federal departments and agencies should identify and share case studies that implement the recommendations in this guide to evaluate the effectiveness of and challenges associated with the recommendations described.

Chapter 1: Introduction

Background

High-activity radioactive sources are in use worldwide for applications in fields including medicine, construction, food processing, and oil and gas.¹ For medical applications, radiation therapy devices for cancer treatment, blood irradiators for prevention of transfusion-associated graft versus host disease (TA-GVHD), and sterilization facilities for medical equipment and food supplies all use high-activity radioactive sources.²

In the late 1990s, as a result of incidents involving radioactive sources and devices that were lost, abandoned, or lacking regulatory control (“orphaned”), the Nuclear Regulatory Commission (NRC) and other domestic and foreign regulatory organizations recognized the need to improve the control over high-activity radioactive sources. Prior to the events of September 11, 2001, the NRC’s regulations focused on the safe use, transportation, and control of licensed radioactive material. The events of 9/11 heightened concerns about the use of high-activity radioactive sources as a radiological dispersal device (or “dirty bomb”) or radiological exposure device in an act of radiological terrorism. As a result, the United States implemented an increased physical security program for radioactive materials that included the existing regulations to maintain the safe use of radioactive materials with enhanced security requirements for those materials deemed “highly risk-significant.”

In 2004, the International Atomic Energy Agency (IAEA) published a revised “Code of Conduct on the Safety and Security of Radioactive Sources,” which provides guidance for the security of radioactive sources throughout their life cycle. The U.S. Government, and 132 other countries to date, made a political commitment to the IAEA Director General to follow the guidance contained in the code of conduct.³ It uses a categorization system for sealed radioactive sources based on their level of risk, categories 1 through 5, as established in IAEA Technical Documents (TECDOCs) 1191 and 1344.^{4,5,6} Category 1 and 2 quantities of radioactive material, if not safely managed or securely protected, would likely cause permanent injury to a person in contact with them for more than a few minutes to an hour for category 1 or hours to days for category 2.⁷

In parallel with ensuring the safe and secure management of sources, non-radioisotopic alternatives have improved in reliability and availability and are, in some applications, a means for achieving

¹ G. M. Moore and M. A. Pomper, “Permanent Risk Reduction: A Roadmap for Replacing High-Risk Radioactive Sources and Materials,” in *CNS Occasional Papers* (Monterey, CA: James Martin Center for Nonproliferation Studies), 2015.

² Centers for Disease Control and Prevention, Office of Public Health Preparedness and Response, “Radioisotope Brief: Cesium-137 (Cs-137),” <http://emergency.cdc.gov/radiation/isotopes/cesium.asp>.

³ See <http://www-ns.iaea.org/downloads/rw/imp-export/status-list.pdf>.

⁴ IAEA, Code of Conduct on the Safety and Security of Radioactive Sources, 2004.

⁵ IAEA, “IAEA-TECDOC-1191: Categorization of Radiation Sources,” (Vienna, Austria: IAEA), 2001.

⁶ IAEA, “IAEA-TECDOC-1344: Categorization of Radioactive Sources: Revision of IAEA-Tecdoc-1191, Categorization of Radiation Sources,” (Vienna, Austria: IAEA), 2003.

⁷ IAEA, Code of Conduct, Annex I.

permanent risk reduction.⁸ The Energy Policy Act of 2005 (Public Law 109-58) directed the NRC to work with the National Academies of Sciences, Engineering, and Medicine to review current industrial, research, and commercial uses of radiation sources and to identify technically and economically feasible replacements for these sources.^{9, 10} In 2008, the National Research Council of the National Academies' Committee on Radiation Source Use and Replacement released its report concluding that the U.S. Government should consider factors such as potential economic consequences of misuse of the radiation sources into its assessments of risk. The committee found that replacing most sources is technically possible, but not necessarily economically feasible.¹¹ The committee also recommended that the U.S. Government take steps in the near term to replace cesium chloride radiation sources, a potential "dirty bomb" ingredient used in some medical and research equipment, with lower-risk alternatives, and that longer-term efforts be undertaken to replace other sources. Additionally, the 2008 National Academies report found that neither sealed source licensees nor manufacturers "bear the full life-cycle cost, including disposal costs, of some of these radiation sources" [National Academies 2008, 9–10]. Moreover, some Federal agencies are bearing the cost of voluntary additional security, transportation, disposal, and environmental remediation of the commercial sector's use of high-activity radioactive sources.

The Energy Policy Act of 2005 also established the Radiation Source Protection and Security Task Force to "evaluate, and provide recommendations relating to, the security of radiation sources in the United States from potential terrorist threats, including acts of sabotage, theft, or use of a radiation source in a radiological dispersal device."¹² The "2014 Radiation Source Protection and Security Task Force Report" noted that "all members support efforts to further reduce security risks by developing alternative technologies as replacements."¹³ The Task Force recommended that U.S. Government agencies, as appropriate, "lead by example" in the consideration and transition to alternative technologies.

The "United States National Progress Report" delivered at the 2016 Nuclear Security Summit highlighted "minimizing nuclear and other radioactive materials" as one of six key focus areas of the United States in strengthening nuclear security implementation. According to the report, "the United States will continue to develop initiatives for reducing the number of vulnerable high-activity radioactive sources through continued research and development on non-radioisotopic alternative technologies, international workshops and collaboration, and direct site engagement."¹⁴ Several Federal Government entities have taken initiatives to encourage U.S. commercial users of radioactive source-based technologies to transition to commercially available alternatives or, where commercially available alternatives do not

⁸ United States Nuclear Regulatory Commission, "Policy Statement of the U.S. Nuclear Regulatory Commission on the Protection of Cesium-137 Chloride Sources," Federal Register Vol.76, No.142, 44381.

⁹ See United States Nuclear Regulatory Commission, "Information Sheet: Radiation Source Use and Replacement Study."

¹⁰ Energy Policy Act of 2005. Public Law 109-58. August 8, 2005.

¹¹ "The committee finds that non-radionuclide replacements exist for nearly all applications of the radiation sources examined, but they may not all now be economically viable or practical." Radiation Source Protection and Security Task Force, "The 2014 Radiation Source Protection and Security Task Force Report," 2014.

¹² Energy Policy Act of 2005.

¹³ Radiation Source Protection and Security Task Force, "2014 Radiation Source Protection and Security Task Force Report."

¹⁴ White House, Office of the Press Secretary, "United States National Progress Report - 2016 Nuclear Security Summit." 2016.

exist, to develop new technologies.¹⁵ These initiatives include a working group of the Department of Homeland Security (DHS) Critical Infrastructure Partnership Advisory Council and an international ad hoc working group on alternatives to high-activity radiological sources.

In 2015, the Interagency Working Group on Alternatives to High-Activity Radioactive Sources (GARS) was chartered and began an assessment of Federal agency involvement with high-activity radioactive sources and development of best practices on how agencies can incorporate the transition to alternative technologies into their strategic plans. This guide is the result of that assessment.

Methodology

GARS examined existing policies, practices, and efforts that encourage or affect the transition to non-radioisotopic technologies. In addition, GARS considered near-term developments that may impact user considerations of and choice between high-activity radioactive sources and non-radioisotopic technologies. GARS also provided a platform for the interagency entities to better understand the interests and concerns of the key stakeholders so that recommendations, to the extent possible, take into account the varying concerns involved in public health and safety, the environment, and national security. This best practices guide provides a summary of recommendations and conclusions of the group as well as guidance on how U.S. Government entities can best transition to or adopt alternative non-radioisotopic technologies, as appropriate.

Scope

The practices presented here focus on high-activity radioactive sources used in medical applications, but these practices may be broadly applicable to other uses of high-activity sources. For the purposes of this document, high-activity radioactive sources are those sources that meet or exceed the category 2 threshold identified in Title 10 CFR Part 37.¹⁶ NRC regulations in Title 10 CFR Section 35.2 define *medical use* as the intentional internal or external administration of byproduct material or the radiation from byproduct material to patients or human research subjects under the supervision of an authorized user.¹⁷ The guidance in this document applies only to processes that either directly or indirectly support clinical care, specifically radiotherapy, sterilization of medical products and instruments, blood irradiation (for preparation of blood components for transfusion), and research irradiation.

The recommendations in this guide are applicable to Federal agencies and departments that perform the following functions:

- procure and use high-activity radioactive sources;
- fund or operate grant mechanisms to academic or commercial entities using high-activity radioactive sources;

¹⁵ For example, starting in 2001, the Environmental Protection Agency (EPA) conducted a comprehensive effort towards the successful implementation of a voluntary alternative technologies initiative (ATI) program to replace devices using sealed radioactive sources in industrial applications. Another initiative is the NNSA Cesium Irradiator Replacement Program (CIRP) (https://nnsa.energy.gov/sites/default/files/nnsa/inlinefiles/DNN_Sentinel_VolII_No1_optimized2.pdf).

¹⁶ See Title 10 CFR Part 37.

¹⁷ See Title 10 CFR Section 35.2.

Transitioning from High-Activity Radioactive Sources to Non-Radioisotopic (Alternative) Technologies

- evaluate, certify, license, or set standards for the use of high-activity radioactive sources, including transportation and disposition; and
- provide security enhancements and end-of-life management of high-activity radioactive sources.

Chapter 2: Summary of Agency Activities

Federal agencies are involved in a variety of activities related to high-activity radioactive sources in various roles. Below are summaries of the GARS member agencies' involvement in these activities.

Department of Agriculture (USDA)

The USDA uses irradiators to sterilize insects in U.S. and Central American programs to eradicate a variety of insects that are harmful to U.S. agriculture. The USDA has also used irradiators to modify physical or chemical characteristics of samples for biological research. The USDA has on-going research and development programs focused on using x-ray technology as an alternative to gamma irradiation for insect sterilization.

Department of Commerce

National Institute of Standards and Technology (NIST)

The Radiation Physics division at NIST owns several radionuclide sources in use to maintain the national standard for air kerma (kinetic energy released per unit mass) and absorbed dose to water. These include category 1 and 2 level sources. One of the primary missions at NIST is to disseminate the air kerma and absorbed dose standard to secondary calibration facilities and end users including: the U.S. Military, Accredited Dosimetry Calibration Laboratories, hospitals, manufacturers of instruments, manufacturers of irradiators, nuclear power plants, Federal agencies, industry, and academic institutions.

The users listed above rely on the standard for air kerma, which is based on both cesium (Cs) and cobalt (Co) radioactive sources (Cs-137 and Co-60), while the standard for absorbed dose to water is based on the use of Co-60 sources. NIST and secondary calibration facilities around the country used these sources to ensure that radiation-measuring instruments measure correctly for a large number of applications. A well-established nationwide network ensures that more than one million instruments are calibrated annually. Annual calibration ensures that the measurements made with these instruments are traceable to the national standard maintained by NIST.

In particular, hospitals and clinics nationwide rely on the Co-60 national standard to ensure that radiation measurements performed in their facilities are accurate. This is critical to ensure that patients undergoing cancer treatment receive the correct dose from any of the multiple types of radiation-based therapy units in hospitals (electron accelerator, X-rays and radionuclide based). A well-established network of calibration facilities based on the use of Co-60 sources exists in the United States to ensure the success of treatment for cancer patients treated with any type of radiation therapy (isotope and non-isotope based).

Department of Defense (DOD)

The majority of DOD medical treatment facilities have removed blood irradiators that contain high-activity radioactive sources. To replace the high-activity radioactive sources, the DOD has encouraged the use of non-radioisotopic x-ray technology to perform blood irradiation. The solution has been effective across the DOD. The DOD continues to work toward permanent risk reduction by supporting new technologies that may eliminate the need for risk-significant radioactive materials.

Department of Energy (DOE)

The U.S. Department of Energy Office of Science oversees the Isotope Development for Production and Research Application Program (the DOE Isotope Program). The mission of the DOE Isotope Program is to produce critical radioactive and stable isotopes that are in short supply, maintain the required infrastructure, and conduct research and development on new and improved methods for isotope production and processing. The DOE Isotope Program serves a broad suite of stakeholders in academia, industry, national laboratories, and the Federal Government. The isotopes produced by the program support both research and applications in different disciplines, including the physical and biological sciences, medicine, defense, national security, and energy. The Isotope Program conducts an annual survey and workshop for all Federal agencies to understand the needs of the Federal complex in terms of isotope demand for successful mission completion, and strives to meet those needs. The Program also mitigates U.S. dependence of critical isotopes on foreign suppliers.

- The DOE Isotope Program produces a variety of radioactive isotopes used in many different medical applications. These are mainly used in small quantities for medical treatment and diagnostic procedures, including actinium-225, radium-223, strontium-82, and strontium-90.
- The DOE Isotope Program does not produce any sealed sources. Within medical applications, the Isotope Program does produce one isotope for use by source manufacturers in category 1 and 2 sources. The Isotope Program produces high specific activity (HSA) Co-60 for medical and industrial applications. DOE produces HSA Co-60 by neutron bombardment of natural cobalt pellets in a high-flux nuclear reactor (the Advanced Test Reactor at the Idaho National Laboratory). This program produces HSA Co-60 to meet approximately 10 percent of global demand under the terms of supply contracts serving domestic commercial sealed source manufacturers. The domestic sealed source manufacturers sell the sealed sources to commercial firms manufacturing and servicing different cancer teletherapy machines used worldwide. An estimated 90 percent of the DOE Isotope Program Co-60 production is dedicated to this application. DOE sells the remaining 10 percent of its Co-60 supply to commercial sealed source manufacturers serving the gamma radiography industry for non-destructive assay. Requests for additional DOE Co-60 product could occur when Canada discontinues production at its NRU reactor.

The Isotope Program is supportive of and encourages the use of alternatives for radioisotopes in all applications, assuming the user (and sponsoring Federal agency, if applicable) has determined that the alternative is economically and technically feasible.

National Nuclear Security Administration (NNSA)

The Department of Energy's National Nuclear Security Administration (NNSA) works with domestic and international collaborators in more than 80 countries to enhance the security of high-activity radioactive sources worldwide. This first-line-of-defense initiative helps prevent unauthorized access to materials for use in a radiological dispersal device ("dirty bomb"), in a radiological exposure device, or for other purposes that could be used in acts of terrorism.

NNSA collaborates with a broad range of stakeholders including government regulatory authorities, responders, industry, and international organizations to enhance the security of medical devices containing high-activity radioactive sources. NNSA uses three strategies under this approach:

- Protection of high-activity radioactive sources used for vital medical purposes;

- Removal and disposition of disused radioactive sources; and
- Reduction of the global reliance on radioactive sources by supporting viable non-radioisotopic alternative technologies.

By supporting the development and use of viable non-radioisotopic alternative technologies, NNSA works toward permanent risk reduction through the elimination of risk-significant radioactive materials. NNSA also works to exchange information on the status of technology, invest in and encourage the improvement of technologies, understand and reduce obstacles preventing implementation, and promote the transition to alternative technologies whenever feasible. NNSA funds research and development in alternative technological solutions where no commercial product exists through its national laboratory and small business innovative research programs.

Department of Health and Human Services (DHHS)

Centers for Disease Control and Prevention (CDC)

CDC has operated high-containment laboratories for medical and public health research on disease-causing microbes since the 1980s. The highest level of containment and most sophisticated laboratory is the biosafety level 4 or BSL-4 laboratory.

Close to the BSL-4 facilities are the irradiator rooms, which house the high-activity self-shielded Co-60 irradiators that provide high-energy gamma rays to sterilize biological material being removed from the facilities for use elsewhere at a lower level of containment. The irradiators also inactivate all of the in-house produced reagents for very high-resolution diagnostics.

Due to the rapid radioactive decay of the Co-60, facilities replace irradiation sources at approximately 5-year intervals to maintain the dosage needed to sterilize materials. Whereas the irradiators are integral to the operation of the BSL-4 facility, the cost of replacement should be included in strategic 5-year planning cycles.

Food and Drug Administration (FDA)

The role of FDA's Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER), together, is to approve radiation-emitting medical devices and to regulate radiation-emitting consumer products. Irradiation of blood is essential to inactivate donor lymphocytes in the blood to prevent TA-GVHD. The first of two types of blood irradiators includes irradiators that contain Co-60 or Cs-137 as a source of ionizing radiation (sealed source irradiators). The second type includes those that use X-ray tubes as a source of ionizing radiation (cabinet irradiators). CDRH consults with CBER for market clearance of blood irradiators via the 510(K) process, which involves a comparison to a legally marketed predicate. The 510(K) process is the likely to be the mechanism for review of all new blood irradiator technology before market clearance. CDRH is responsible for the pre-market review of all radiation-emitting medical devices via the medical device regulations and the electronic product radiation control (EPRC) regulations. The EPRC regulations specifically cover any electronic sources of ionizing and non-ionizing radiation. CBER currently has a guidance document that covers the use of ionizing radiation for the irradiation of blood. Post-market requirements for radiation emitting products and radiation emitting device manufacturer compliance are the responsibility of the Division of Radiological Health within the Office of In-Vitro Diagnostics and Radiological Health.

A firm that wants to make licensed irradiated products needs a Prior Approval Supplement (PAS), which is a process-specific approval. After receiving a PAS for one product, the firm has authority to irradiate

other products and only send in labels. For the PAS supplement, FDA reviews the standard operating procedures, labels, dose maps, 2 months of production records, etc. FDA relies on a compliance check in lieu of an inspection provided that the most recent inspection included a review of the irradiation activities and there were no compliance problems at the firm. Once the firm has a license for irradiated products, FDA's Office of Regulatory Affairs will cover the firm during its routine inspections.

National Institutes of Health (NIH)

NIH comprises 27 individual Institutes and Centers that together constitute the Federal Government's biomedical research agency. The NIH Intramural Research Program employs about 6,000 scientists and hosts many thousands of fellows to further scientific discoveries in basic, clinical, and translational biomedical research. The NIH Office of Extramural Research funds numerous research grants to provide more than 80% of the NIH budget to over 300,000 research personnel at over 2,500 universities and research institutions in the United States and around the world. Some medical devices that support the NIH's medical research mission contain high quantities of radioactive material. As such, NIH procures such devices to meet its mission needs either through approved grants using Intramural Research funds or Extramural Research funds. In this way, end users of the devices are able to accomplish the goals of a wide variety of research and clinical protocols and, in so doing, advance the NIH research mission. Examples may include Cs-137 irradiators for the irradiation of blood products; for the irradiation of research animals as a means to create a chimeric animal model; for the irradiation of cells as a method of studying DNA damage or of controlling their proliferation; and gamma knife radiosurgery devices for the precise treatment of solid cancers.

Institutes in the Intramural Research program procure these devices in accordance with the NIH license issued by the NRC to possess and use high-activity radioactive sources. Currently, the NIH license authorizes multiple self-shielded irradiators (Cs-137 and Co-60). NIH has one blood irradiator (Cs-137 based), and many cesium, cobalt, and X-ray irradiators in use in research applications. The number of irradiators or other category 1 or 2 devices Extramural Research grantees procured is uncertain. The NIH Intramural Research license does not cover any devices procured through the Extramural Research grants program, and grantees are required to apply for and receive their own licenses to possess and use the devices in accordance with NRC or Agreement State requirements.

Whether procurement of irradiators is through the Intramural or the Extramural Research program, appropriation of funds is the same as for any large equipment purchase for a research study. Typically source reload and disposal costs are not itemized in the same procurement transaction in which the device is initially purchased, and funds are not set aside for the future because these expenses are not needed for many years (sometimes decades) after the initial purchase, and funds are allotted for the fiscal year in which they are needed.

Centers for Medicare and Medicaid Services (CMS)

The Centers for Medicare & Medicaid Services (CMS), a Federal agency and branch of the U.S. Department of Health & Human Services, administers Medicare, Medicaid and the Children's Health Insurance Program in collaboration with state governments and private health insurance programs including Health Insurance Marketplaces, and provides information for health professionals, regional governments, and consumers. From a CMS perspective, reimbursement for a procedure that uses a non-radioisotopic alternative device poses no problem as long as FDA has granted proper clearance for the procedure. Little to no impact is associated with reimbursement for a procedure for the support services (e.g. medical sterilization) this guide covers. CMS typically does not provide a differential if existing

technologies have different costs. This means that early adopters of an alternative technology would have to cover additional costs above the reimbursement cost for the activity using radioactive source technology. The reimbursement cost for the use of any technology as part of a procedure is based on the market determination of an average cost for the use of a technology and an associated cap on total expenditures (e.g., physician cost, malpractice cost, and office cost). Periodic recalculations of these costs occur every 5–10 years.

Department of State

The U.S. Department of State develops and coordinates bilateral and multilateral efforts to secure radioactive sources and provide incident response assistance. The Department of State specifically develops and coordinates U.S. policy as it relates to: 1) international standards, and working with international collaborators to encourage meeting these standards, 2) guidance and practices related to radiological safety and security, 3) transfers of high-activity radioactive sources across borders, and 4) incident response.

Department of Veterans Affairs (VA)

In total, the VA has six remaining facilities that have high-activity radioactive source-based irradiators. The VA is aware that several facilities have switched from high-activity source irradiators to non-radioactive alternatives. The initial feedback on these systems is that the longer-term operation and maintenance costs are a challenge and may be an obstacle to change.

Environmental Protection Agency (EPA)

The Radiation Protection Division (RPD) in the EPA Office of Radiation and Indoor Air (ORIA) is responsible for administering specific provisions of the Clean Air Act, the Atomic Energy Act, and the Waste Isolation Pilot Plant Land Withdrawal Act, among other applicable environmental rules and regulations concerning radiation hazards. ORIA's fundamental mission is to protect the public and the environment from the risks of exposure to radiation sources including indoor Radon. The office coordinates across the Agency and with other Federal, State, and tribal organizations, including international governmental and non-governmental organizations, to carry out its mission. RPD is the designated entity to perform radiological risk assessment to determine the overall risks and impacts of radiation on public health and the environment, including indoor air environments, and in particular to monitor the ongoing activities at the Waste Isolation Pilot Plant (WIPP). In addition, every 5 years RPD conducts a recertification of WIPP's compliance with EPA's radioactive transuranic waste disposal standards.

Distinctively, the RPD develops criteria, standards, guidance, policies, and programs to limit and control unnecessary exposure to radiation and radioisotopic pollutants. For example, it develops technical reports to help standardize methods for dose and risk assessment, available to the relevant communities. Other functions encompass directing a nation-wide environmental radiation monitoring program known as RadNet; and collaborating globally with counterparts in monitoring uncontrolled accidental radiation releases from nuclear power plants (e.g., Fukushima, Chernobyl) by providing the necessary technical support and assets in coordination with other Federal responders to radiological emergencies. During response to emergencies, the EPA's Radiological Emergency Response Team works with Federal, State, and local agencies to monitor and clean up affected areas and applies its protective action guidelines to help determine what actions are necessary to protect a population from unhealthy levels of radiation.

Of note, EPA regulates orphan radioactive material that has fallen out of control and is of unknown origin and unlicensed rad source or material for which the current or former licensee holder is not financially viable or otherwise unable to control the material. To deal with this problem, in 2001 RPD established a Voluntary Alternative Initiative (ATI), which grew out of this set of circumstances. In a collaboration with government, industry, researchers, and end-user stakeholders, the goal of ATI was to reduce the number of sealed sources used in industrial applications by substitution with non-radioisotopic alternatives that are technically and economically advantageous, taking the entire life cycle into consideration. RPD worked very closely with all stakeholders to identify and address issues and barriers necessary for successful implementation. This programmatic strategy included market demonstration projects for devices that are available or near entering the market place and conducting verification studies supported by the EPA Environmental Technology Verification under the auspices of the EPA Office of Research and Development. All new technologies emphasized by these projects had to meet the NIST, ANSI, and other user-specific requirements or standards.

Nuclear Regulatory Commission (NRC)

NRC does not use or procure medical devices containing byproduct material.¹⁸ The NRC's mission is to regulate the Nation's civilian use of byproduct, source, and special nuclear materials to ensure adequate protection of public health and safety, to promote the common defense and security, and to protect the environment. The byproduct materials that the NRC and the Agreement States¹⁹ regulate are used for medical, industrial, and academic purposes. Nationwide, the NRC and Agreement States regulate approximately 21,000 licensees; the NRC regulates 3,000 of those.

The NRC maintains oversight over Federal departments and agencies using byproduct material. The NRC does not relinquish this authority to an Agreement State.

Domestically, the NRC and Agreement States regulatory framework provides a baseline level of safety and security in accordance with 10 CFR Part 37 and provides additional guidance to licensees regarding best practices beyond the requirements. The key requirements of the security program for category 1 and 2 materials include:

- Pre-licensing by the regulator. Activities include screening criteria and visiting sites for new applicants before a license is issued; processing requests for an increase in possession limits to quantities above category 2 (subject to additional screening and a site visit); and verifying 10 CFR Part 37 implementation before authorizing receipt of quantities above category 2.

¹⁸ The Atomic Energy Act, as amended in 1978 and in 2005 by the Energy Policy Act, defines byproduct material in Section 11e.(1) as radioactive material (except special nuclear material) yielded in or made radioactive by exposure to the radiation incident to the process of producing or using special nuclear material. According to the NRC definition, "source material" means either the element thorium or the element uranium (not enriched in U-235). Source material also includes any combination of thorium and uranium, in any physical or chemical form, or ores that contain by weight one-twentieth of one percent (0.05 percent) or more of uranium, thorium, or any combination thereof. Depleted uranium (left over from uranium enrichment) is a source material. Title I of the Atomic Energy Act of 1954 defines "special nuclear material" as plutonium, uranium-233, or uranium enriched in the isotopes uranium-233 or uranium-235. The definition includes any other material that NRC determines to be special nuclear material, but does not include source material. NRC has not declared any other material as special nuclear material.

¹⁹ Agreement States are States in the United States that have signed agreements with the NRC to regulate certain uses of radioactive materials within those States.

- Background checks. For example, fingerprinting helps ensure that individuals with unescorted access are trustworthy and reliable.
- Personnel access. Access to areas where radioactive material in quantities of concern are stored and used must be limited to individuals deemed trustworthy and reliable, based on background and criminal history checks, and a legitimate need for access.
- Documented security programs designed with a layered defense to detect, assess, and respond to actual or attempted unauthorized access.
- Coordination and response. Planning is between the licensee and local law enforcement agencies for the licensee's jurisdiction.
- Shipping. Coordination and tracking of radioactive material shipments include the shipper.
- Verification. The regulator verifies that the receiver has authority to possess the types and quantities of transferred materials. The NRC maintains the License Verification System to allow a licensee to conduct this verification with the regulator securely through an on-line system. (Integration of the National Source Tracking System (NSTS) and Web-based licensing systems allowed for combined license verification, i.e., a check of both the license validity and a check of the NSTS inventory).
- Security barriers. Additional security barriers as needed to prevent theft of portable devices.
- Effective management of the National Source Tracking System (NSTS). NSTS is a national registry to track and account for category 1 and 2 sources from cradle to grave.

Ultimate responsibility for the safety and security of radioactive materials in the United States rests with the licensees that possess these materials. To assist in that effort, the Department of Energy (DOE) and National Nuclear Security Administration (NNSA) work with the NRC; Agreement States; the materials licensees; State, local and tribal governments; and other Federal agencies to build on the existing regulatory requirements by providing voluntary security enhancements.

Chapter 3: State of Alternative Technologies R&D

Commercial alternatives to high-activity radiation sources are available for medical applications including radiotherapy, sterilization of medical devices and supplies, blood irradiation, and research irradiation. This chapter provides an overview of user requirements for those medical applications and then describes the currently available technologies and ongoing research and development for non-radioisotopic alternatives for each of the four medical applications.

Table 1: Overview of Category 1- and 2-Based and Alternative Technology-based Devices Used in Medical Applications

Application	Typical Source(s)	Potential Alternative*
Radiotherapy	Co-60	Linear Accelerators
Medical Instrument Sterilization	Co-60	Linear accelerators producing electron beams , X-rays, X-ray tubes
Blood Irradiation	Cs-137, Co-60	X-ray tubes, linear accelerators, UV pathogen reduction technology**
Research Irradiation	Cs-137, Co-60	X-ray tubes***

*Depending on user-specific needs and resources.

** Not yet approved by the U.S. FDA for treatment of red blood cells.

*** Not currently feasible in some cases. See text for details.

User Requirements and Considerations

Users of some FDA-regulated devices require a standard radiation dose. For example, the FDA has established a radiation dose minimum for blood products in order to prevent TA-GVHD.²⁰ In addition, blood irradiators must also meet the end user's requirements for reliable function, efficient throughput, and minimal down time for repairs/maintenance. In a clinical environment, access to a working irradiator is critical to provide irradiated blood products for patients at risk for TA-GVHD. Pre-irradiation of blood products severely limits their shelf life, so timely and prompt irradiation is the standard of care.²¹

Some Federal agencies, such as NIST, have mission-specific requirements that mandate the continued use of Cs-137 and Co-60 as irradiation sources, for the development of calibration standards to quantify air kerma and absorbed dose in tissue.

²⁰ Food and Drug Administration (FDA) Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products, 1993.

²¹ Ibid. Studies have shown irradiated blood products to have satisfactory storage lives limited to 2-5 weeks post-irradiation, but have not shown gamma irradiation below 50Gy to have a significant clinical change in platelet function. See, for example, J. Chapman et al., "Guidelines on Gamma Irradiation of Blood Components for the Prevention of Transfusion-Associated Graft-versus-Host Disease," *Transfusion Medicine*, 6 (1996): 261–271.

Users should determine if use of radionuclide sources alone will meet their technical needs or if some alternative technology can provide a viable option. Considerations may be the different radiobiological effectiveness (RBE) between the two technologies, the technology's ability to achieve uniformly the required radiation dose and dose rate needed, and the ability of the technology to offer a chamber size able to fit the sample. End users who have already invested in an irradiation technology will need to consider the costs and benefits of their current usage compared with a potential new technology, especially given the significant capital investment.

A conversion from a radioactive source device to an alternative technology would require an analysis of current operational cost (maintenance, source replacement, training, decommissioning, disposition, license cost, regulatory requirement of security and inspections) as well as projected cost of alternatives (new equipment, maintenance, facility modifications, training, source disposition, decommissioning).

Clinical trials and efficacy testing will be necessary to compare new alternative technologies side by side with existing technologies. Where possible, the publication of results of such tests will help inform the user community.

Radiotherapy

Technical Specifications

Radiation therapy is one of the primary methods used to treat cancer anywhere in the human body. Approximately 50–60% of all cancer patients will receive radiation therapy in one form or another. Radiation therapy uses ionizing radiation to inhibit the proliferation of defective cells such as those found in cancer. The radiation must be highly focused and precisely controlled in terms of energy, intensity, and location. Therapeutic radiation can come from complex electronic machines or radioisotopes.

Current State of Radiotherapy

There are several methods currently used to deliver radiation to cancers in the human body. However, external beam radiation therapy is the only method relevant to this document.

External beam radiation therapy (also known as teletherapy) uses complex electronic medical devices to produce radiation outside the body and target tumors inside the body. These devices can also include on-board imaging, sensitive tumor-movement tracking systems, and dynamic beam collimation devices. Linear accelerators are the most widely used form of external beam radiation therapy. Commercially available linear accelerators are widely used for radiotherapy. In the United States and other developed countries, accelerators have mostly replaced Co-60 irradiators in external teletherapy applications. Despite this transition, many radioisotope-based devices are still in use, particularly for the subset of teletherapy known as stereotactic radiotherapy and stereotactic radiosurgery. Depending on requirements, physicians may also use linear accelerators for stereotactic radiosurgery or stereotactic radiotherapy in many treatment applications.

Cobalt-60 (Co-60) is the primary isotope used in large radioisotope-based medical irradiators. For example, a widely used stereotactic radiosurgery device uses about 200 individual Co-60 sources to converge gamma radiation beams at a focal point in a patient's head and neck tumor. This configuration lessens damage to healthy tissue while still delivering a high dose to the target. Medical practitioners also use Co-60 in a similar configuration, in combination with magnetic resonance imaging, to provide real-time imaging during radiation therapy. Practitioners use Co-60-based devices in some specialized

radiosurgical applications when such applications would best meet specific treatment requirements. This may include instances when radiation is needed near a critical tissue structure, requiring sharp radiation fall-off. Therefore, complete adaptation of alternative technologies in radiosurgical applications is unlikely.

Other forms of external beam radiotherapy include devices that accelerate protons or heavy ions (e.g., carbon ions), which practitioners can then precisely control to target tumors located close to critical normal tissue structures in the human body.²²

Current Government Involvement

NNSA's Office of Research and Development under the Office of Defense Nuclear Nonproliferation currently funds no projects for this specific application.

Federal agencies who service a patient population, such as the NIH, VA, and DOD military hospitals, may employ some of these devices to treat different forms of cancer, but no Federal agency is currently in possession of stereotactic radiosurgery devices. Alternatives exist in the form of linear accelerators, which uses an X-ray beam instead of the gamma emission of a radionuclide, as well as electron, proton or neutron accelerators. Differences of opinion exist in the field of radiation oncology on the relative superiority of these different devices, due to the various therapeutic advantages and disadvantages of the different technologies and devices. Furthermore, the technologies may have notable differences in operations and performance to the end user. Radiological materials security concerns are applicable only to the radionuclide source technologies. From a cost perspective, both radionuclide-containing devices and devices utilizing alternative technologies are major investments and purchase and installation costs for either class of device are comparable.

Medical Instrument Sterilization

Technical Specifications

The FDA requires sterilization of all invasive medical and dental devices. Sterilization of single-use medical instruments requires consistent and penetrating radiation sufficient to kill any pathogens present and a radiation intensity that allows for timely processing.

Current State of Medical Instrument Sterilization

Medical device sterilization primarily occurs in radioisotope-based panoramic irradiation facilities, although electron beam and X-ray tube technologies may also be used. Of all devices that utilize radioactive sources, panoramic irradiators contain sources at the highest levels of activity, which is typically about 110,000 TBq (terabecquerel) or 3 million Curies (Ci). Mostly due to these high-activity irradiators, approximately 98 percent of civilian source activity in the United States is in the form of Co-60.

Several alternative technologies for the sterilization of medical instruments (e.g., X-ray, electron beam, heat, and ethylene oxide) are currently being developed and refined. Typical X-ray tubes or accelerators

²² HDR brachytherapy devices utilize radionuclide source technology, and frequently contain a single source of Ir-192, ranked as a Category 3 device (outside of the scope of this guide). However, multiple HDR brachytherapy devices, if co-located, would elevate the aggregated Ir-192 sources to a Category 2 level, and increased security controls would apply. Other HDR devices may contain Co-60 as their choice of brachytherapy source.

used as high-intensity photon sources would provide the most straightforward replacements because the radiation penetration is similar to that of radioisotope-based technology. X-ray sterilization systems are now commercially available but are not yet in wide use. A 5-year cost assessment study conducted by a manufacturer of X-ray sterilization facilities found that X-ray would be more economical for construction of a brand new facility than gamma sources above that of 55 MBq would be. The United States does not have an X-ray facility capable of achieving 55 MBq, which is equivalent to that of large-scale gamma sources. The manufacturer has acknowledged that most medical device manufacturers would require at least two facilities within a reasonable radius to serve as backup for each facility to ensure business continuity. In addition to the cost of building an X-ray sterilization facility, medical instruments would have to undergo revalidation studies to ensure sterilization equivalency and lack of material alteration.

The gamma penetration of radioisotope-based technologies is effective in low-density items and also in high-density items. The primary challenge of an alternative technology-based device is to provide sufficient penetration for a wide variety of sizes, shapes, and materials. In addition, processing time must be the same or less than current commercial radioisotope systems.

A particle accelerator can generate a directed electron beam for use in sterilization. Due to its limited penetration, the electron beam approach is best suited to thin, low-density materials. This technology is currently in use in several large-scale facilities.

Heating and exposure to ethylene oxide are two simple and well-established sterilization techniques for medical devices. Steam autoclaves or dry ovens can sterilize reusable medical items, but these methods are not ideal for single-use items due to the damage they cause to plastic. Ethylene oxide exposure has been in use for several decades to sterilize medical devices, but operational issues, including equipment complexity, toxicity, flammability, and explosive hazards, make the ethylene oxide approach difficult to deploy.

Current Government Involvement

NNSA's Office of Research and Development under the Office of Defense Nuclear Nonproliferation currently funds technology development of an X-ray source based on a compact superconducting linear electron accelerator to replace large gamma ray sources for bulk sterilization of medical equipment. Superconducting linear accelerators offer higher beam power, much higher efficiency, and potentially lower operating costs than traditional accelerators, though they are more complex and require cryogenic cooling. This research and development aims to demonstrate the increased reliability and lower operational costs required to make this technology commercially competitive.

No Federal departments or agencies currently have license to operate panoramic irradiators for the sterilization of medical devices or supplies.

Blood Irradiation

Technical Specifications

Patients with hematological malignancies, immunocompromised patients, premature infants and other selected patients are required to have blood products irradiated before transfusion.²³ Donor

²³ <http://www.bloodjournal.org/content/early/2015/04/29/blood-2015-01-620872>

lymphocytes are the causative agent of TA-GVHD, a rare but often lethal complication of blood transfusion. Federal agencies rely on a 1993 memorandum that discusses expectations regarding the irradiation of blood products.²⁴ For gamma irradiators, a radiation dose of 25 Gray (Gy) delivered to the central portion of an irradiation canister, with a minimum of 15 Gy delivered to the periphery of the canister, has been shown to completely inactivate donor lymphocytes without unduly affecting other blood components.²⁵

Current State of Blood Irradiation

Cs-137 irradiators and, to a lesser extent, Co-60 irradiators, have been used for decades to inactivate donor lymphocytes. As concerns about category 1 and 2 devices have increased, there have been efforts to identify alternative technologies to Cs-137 and Co-60 blood irradiation devices. Blood irradiation devices have proven to be reliable, easy to maintain, and have long operational life spans.

Non-radioisotopic alternatives for blood irradiation applications include:

- **Leukocyte Reduction:** High-efficiency filters remove >99% of donor lymphocytes. Not recommended, as viable lymphocytes can be transfused and cause TA-GVHD.
- **Pathogen Reduction Technologies:** Technologies using various additives and UV-light inactivate all lymphocytes. However, approved only for platelets and plasma. Gamma or X-ray Irradiation is required for red blood cells.
- **X-ray Irradiation:** Effective alternate to gamma irradiation used at some blood centers. There are major cost constraints restricting conversion of existing gamma irradiators to x-irradiators.

In the United States, X-ray irradiation has emerged as a viable alternate technique for inactivating donor lymphocytes in blood products being prepared for transfusion. X-ray irradiators aimed at the blood transfusion market have been for sale in the United States since the early 2000s. Many end users report a high level of satisfaction with these devices. Newer models of X-ray irradiators have lessened concerns about elaborate plumbing, cooling requirements, and frequent breakdowns.

The blood collection, processing, and distribution system in the United States is currently under severe financial pressure, as the transfusion of blood diminishes secondary to better blood management techniques adopted by hospitals. There are reports of a greater need for quality control for X-ray irradiators than gamma irradiators and maintenance needs may be more complex as well. Cost is fairly equivalent between the two systems, although there will be added cost for facilities who wish to convert from gamma to X-ray (e.g., possible facility renovation, cesium disposal cost).

Pathogen reduction technology (PRT) is also effective at inactivating donor lymphocytes in addition to preventing or reducing the occurrence of transfusion-transmitted infections and bacterial pathogen contamination. This method introduces into blood products agents that damage lymphocyte nucleic acids upon exposure to ultraviolet light. In 2014, the FDA approved two UV systems to treat plasma and platelets for pathogen and bacterial reduction. The approved systems use the UVA wavelength range of

²⁴ Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products, 1993.

²⁵ Ibid. The requirement that the “dose of irradiation delivered should be 2500 cGy targeted to the central portion of the container and the minimum dose should be 1500 cGy at any other point” is based on studies done with a sealed source blood irradiator with a single pencil source and a turntable rotating the blood component and canister.

illumination with the molecule amotosalen, which interacts with nucleic acid. While UV systems are not yet FDA-approved for TA-GVHD prevention, the AABB modified its U.S. standards in 2016 to indicate that use of licensed pathogen reduction systems meets the standard for prevention of TA-GVHD. A red cell system needs FDA approval in the United States before UV systems could replace Cs-137 systems. Because PRT is not currently a treatment for red blood cells, blood establishments must have an alternate method for inactivating lymphocytes in this widely used blood product.²⁶ Table 2 provides an overview of the approved applications and treatments each type of irradiation device achieves, based on information gathered by a related working group of the DHS Critical Infrastructure Partnership Advisory Council.

Table 2: Comparison of Devices for Blood Irradiation by Application and Outcome

Key: ✓ CE Marking & FDA approved for use (✓) CE Marking only for use (cannot be sold in United States)	Isotopic Technology	Non-radioisotopic Alternative Technologies		
	Gamma (Cs-137) Irradiator	X-ray Irradiator	UV Pathogen Reduction ¹ (Amotosalen)	UV Pathogen Reduction (Riboflavin)
Whole Blood	✓	✓		(✓)
Platelets	✓	✓	✓	(✓)
Plasma	✓	✓	✓	(✓)
Red Blood Cells	✓	✓		
Transfusion-Associated Graft vs. Host Disease (T-Cell Inactivation) ²	✓	✓	(✓)	(✓)
Transfusion-Transmitted Infections ³			✓	(✓)
Transfusion-Associated Adverse Reactions ⁴			✓	(✓)

¹ One manufacturer uses two separate systems to treat platelets and plasma separately. Both systems received FDA approval in December 2014. Other manufacturers should be entering the U.S. market soon.

² CE Marking incorporates recognition that these technologies may be used for the prevention of TA-GVHD.

³ Examples of transfusion-transmitted infections include enveloped viruses (i.e., Chikungunya, Dengue, and Influenza A), non-enveloped viruses (i.e., parvovirus B19, feline calicivirus, and human adenovirus 5), gram-negative bacteria (i.e., *Klebsiella pneumoniae*, *Yersinia enterocolitica*, *Escherichia coli*, and *Salmonella choleraesuis*), gram-positive bacteria (*Staphylococcus epidermidis*, *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Listeria monocytogenes*), spirochetes (i.e., *Treponema pallidum* and *Borrelia burgdorferi*), and protozoa (i.e., *Trypanosoma cruzi* and *Plasmodium falciparum*).

⁴ Transfusion-associated adverse reactions include allergic transfusion reactions, febrile transfusion reactions, and immunization to human leukocyte antigens.

Current Government Involvement

NNSA’s Office of Research and Development under the Office of Defense Nuclear Nonproliferation is currently funding research to develop flat-panel X-ray sources for use in blood irradiation applications. The resulting irradiators should be about the size of a microwave oven, weigh between 200 and 500 pounds, operate on 110 AC power for the small (two 400-ml bags in four minutes) and medium (four

²⁶ AABB Association Bulletin #16-05, “Changes to the 30th Edition of Standards for Blood Banks and Transfusion Services,” March 17, 2016, <https://www.aabb.org/programs/publications/bulletins/Documents/ab16-05.pdf>.

bags) models, operate on 220 single phase for the large (six bags on a tray or conveyor) models, require no external cooling, and be extremely reliable.

Research Irradiation

Technical Specifications

Many Federal departments and agencies use research irradiators for a variety of purposes. These irradiators commonly contain Cs-137 or Co-60 radiation sources in category 1 or 2 quantities. For animal irradiation, the irradiation method must avoid pain and distress for the animal. For cell irradiation in support of cancer treatment applications, the technology must achieve the desired depth dose requirements.

In some cases, research is founded on the specific photopeak radiological emissions from energies specific to the isotope; radionuclide energy sources (as in Cs-137 and Co-60) are photopeak energy sources, meaning that their energy emissions are at a unique energy level. In other cases, the end user may simply need a source of high-energy photon emission to provide a radiation dose to a sample. In the former situation, no current alternative technology will directly substitute for the Cs-137 or Co-60 emission; a new technology is necessary to provide a specific energy. In the latter situation, it is possible that alternative X-ray or linear accelerator technology can substitute. In other words, the difference between a 662 keV energy emission (Cs-137), a 2.5 MeV energy emission (Co-60), and a 160 kVp energy emission of currently available X-ray tubes will not matter as long as the total amount of energy deposited at the sample depth needed is sufficient for the researcher.²⁷

X-ray sources are spectrum energy emissions, meaning that their energy emits over a range of energies up to the maximum kVp. The lower energies cannot penetrate as far into a sample as the higher energies and so the target absorbs lower energies without providing a dose to the sample depth. Thus, in practice, filters limit the lowest energies so that only the more highly penetrating energies are delivered, although at a loss of dose rate. For example, an unfiltered X-ray beam of 160 kVp may give 60 Gy/min to the sample chamber, while a filtered (2 mm Aluminum) beam of 160 kVp may only give 6 Gy/min to the same chamber. X-ray beam filtration is important especially for small animal research, due to the damaging impact of the shallow X-ray energy deposition on the animal skin. Dermal burns have been reported when filtration is not adequately used. Commercial X-ray irradiators in current use in the U.S. offer X-ray tubes of 160 kVp, 225 kVp, or 320 kVp, which can provide up to the order of 15 Gy/min. Cesium-137 irradiators can provide that equivalent dose rate and higher, while Co-60 irradiators provide on the order of hundreds of Gy/min.

When switching to an alternative technology, many researchers will need to repeat baseline experiments with the new technology in order to demonstrate reproducible results equivalent to the cesium technology or to determine a weighting factor to describe differences in outcomes. Biomedical researchers, in particular, may not be easily swayed by proclamations of success by others and are apt to take a rigorous approach to determining whether duplication of prior research results is necessary.

²⁷ The unit kVp refers to "kilovoltage peak." It describes both the accelerating voltage of the accelerator and the resulting energy of accelerated electrons. As an example, a 500 kVp accelerator would produce electrons with 500 keV of energy. These electrons can interact with a target to create bremsstrahlung x-rays of a broad energy spectrum up to the electron energy.

Current State of Research Irradiation

For irradiation of small animals (mice) and mammalian cells, currently available X-ray irradiators provide an equivalent alternative to cesium or cobalt.²⁸ For larger animals (rats) and radio-resistant organisms such as bacteria, current X-ray irradiators will not achieve the required dose rate at the target sample depth needed.

An informal survey at the NIH of 25 current users of Cs-137 irradiators and at the CDC of nine current users of Co-60 irradiators found a wide range of feedback regarding the question of switching to alternate (X-ray) technology. The appendix to this guide contains details. NIH grouped responses into five categories: users unwilling to switch since duplication of experimental results are necessary; users willing to conduct repeat of experimental results and switch to X-ray if results show no difference; users already predicting it's okay to switch to X-ray; users unwilling to switch since they predict X-ray will not produce the same results; and users unwilling to switch since they predict that X-ray will not permit the same throughput. Of the 34 respondents, the majority (56%) were willing to immediately switch, or were willing to test reproducibility and switch if satisfied. The remaining 44% expressed unwillingness to switch to or even try alternative technologies for various reasons.

Users did not typically consider cost or operational concerns. Instead, their focus was primarily on the technological feasibility of switching from cesium to X-ray. However, all of these factors would come into play if the theoretical switch becomes a reality.

Current Government-Funded R&D

NNSA's Office of Research and Development under the Office of Defense Nuclear Nonproliferation is currently funding a research irradiator using flat panel X-ray source.

One new technology is under development using an X-ray flat screen that will enable different doses to separate samples irradiated at the same time, for small samples such as cells. This development would provide a unique capability that some researchers would find valuable.

²⁸ These X-ray irradiators are replacement for either category 1 or category 2 sources.

Chapter 4: Government Role in Promoting Alternative Technology

The 2014 Radiation Source Protection and Security Task Force (Task Force) report to Congress recommended that U.S. Government departments and agencies, as appropriate, lead by example in the consideration and transition to lower-risk radiological or non-radioisotopic alternative technologies. Departments and agencies will have varying levels of direct and indirect utilization and management of source-based or non-radioisotopic devices. Nevertheless, several different regulatory, policy, and programmatic measures exist that influence respective users' decisions to transition to alternatives.

This chapter provides an overview of different approaches the Federal Government may consider to facilitate the adoption of alternative technologies, as well as the inclusion of a case study. The policies suggested represent some of the measures that agencies may consider, but should not be viewed as specific recommendations for any particular agency. See the Recommendations section of the report for GARS members' recommendations.

Federal Procurement or Grant-Making Approach

Some agencies have a role in direct procurement of source-based devices for Federal ownership or usage, others in the grant-making process for procurement and distribution of devices for intramural or extramural research purposes. These agencies should consider establishing internal policies and practices for evaluating or facilitating acquisition of non-radioisotopic alternative technologies.

For example, under NNSA's voluntary Cesium Irradiator Replacement Program (CIRP), the Office of Radiological Security collaborates with commercial licensees to replace their Cs-137 irradiators with X-ray irradiators. Through CIRP, NNSA provides a financial incentive toward the purchase of an X-ray irradiator, contingent on the disposition of the Cs-137 irradiator at the site. Disposition is facilitated through NNSA's Off-site Source Recovery Program (OSRP).

The following are examples of policy measures that agencies with a direct role in funding or procuring source-based devices for medical applications should consider:

- Establishing grant programs to conduct clinical trials required for alternative technologies that will be used in direct and indirect human health care;
- Setting internal policies to no longer purchase source-based devices, discontinue the use of, or terminate provision of grant funds for their purchase;
- Requiring end-users or grant applicants to provide a justification why their intended irradiator purchases are required, and to identify objectives that cannot be fulfilled by a non-radioisotopic alternative;
- Identifying relevant emerging issues such as the development of standards;
- Instituting internal protocols or policies to phase out the use of an existing device(s);
- Designing the necessary procedure(s) to accelerate implementation of non-radioisotopic replacements as the devices reach the end of their useful life, or as organizational needs or directions change; and
- Providing diverse and timely incentives to encourage the early transition to non-radioisotopic technology prior to the end-of-life of the source-based device.

Regulatory Priorities Approach

Although they are not involved in the direct funding or procurement of source-based devices, agencies with regulatory authority have a key role in promoting information sharing about both the phase-out of isotopic device(s) and the emergence of non-radioisotopic alternatives. These agencies also fund, oversee, or review the results of the field and clinical trials that will test the alternative technologies. In addition, those agencies could consider policies and programmatic goals designed to influence the discontinued ownership and use of a source-based device when and where possible.

Policy measures or programmatic actions for agencies may include:

- Supporting a voluntary, standardized system designed with pre-defined parameters for tracking non-radioisotopic devices, especially blood and research irradiators, to promote increased awareness of the market availability and sources (vendors, manufacturers, etc.) or distribution centers of the devices;
- Evaluating Federal licensing or reimbursement structures for usage of source-based or non-radioisotopic devices across applications (e.g., blood products);
- Developing and promoting Government-wide uniform regulations and standards;
- Expediting approvals or supporting the market entrance, where possible, of non-radioisotopic devices entering the commercial market;
- Reviewing marketplace for performance, operational successes, and challenges;
- Providing informational updates to agency stakeholders when new source-based or non-radioisotopic devices enter the market;
- Facilitating the process of transitioning to and the acquisition of non-radioisotopic devices while limiting the use and storage of isotopic devices; and
- Requiring licensees to cover costs associated with source disposition (UK, Canada, France).^{29, 30, 31, 32, 33}

Policy measures that have been internationally implemented but that may not be viable in the United States include:

²⁹ European Union, "Control of High-Activity Sealed Radioactive Sources in Europe: Implementation of Directive 2003/122/EURATOM in EU-27 and the Current EU Regulatory Development Activities," Commission Staff Working Document [SWD/2015/0084 final] <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52015SC0084>.

³⁰ Canadian Nuclear Safety Commission, Licensing Process: Financial Guarantees, <http://nuclearsafety.gc.ca/eng/nuclear-substances/licensing-nuclear-substances-and-radiation-devices/licensing-process/financial-guarantees/index.cfm>

³¹ "Considerations for the Adoption of Alternative Technologies to Replace Radioactive Sources." World Institute for Nuclear Security, 2016.

³² "Considerations for the Adoption of Alternative Technologies to Replace Radioactive Sources." World Institute for Nuclear Security, 2016.

³³ Australia requires that licensees provide "a plan for the ultimate transfer or disposal of sources," but the Working Group could not determine whether such a plan required licensees to cover costs associated with source disposition. (See <http://www.arpsansa.gov.au/pubs/regulatory/guides/REG-LA-SUP-240E.pdf>)

- Requiring licensees to provide a justification why their intended use cannot be fulfilled by a non-radioisotopic device, instead of the source-based device (Norway, France, and Belgium)^{34, 35}
- Considering a phased licensing approach to not re-license older devices after a certain timeframe, or not consider new devices for license (France)³⁶
- Requiring licensees to buy into an insurance policy (Canada)³⁷

Education and Outreach Approach

Agencies without a direct role in the procurement or regulation of high-activity radioactive sources may play a role in educational or outreach efforts to industry and commercial stakeholders of applications for both source-based and non-radioisotopic devices. Although motivations may be quite different (e.g., research, national security, clinical treatment, etc.), this area is where departments and agencies can lead by example to easily demonstrate cooperation and collaboration in the user community.

Examples of educational and outreach efforts may include:

- Supporting increased information-sharing on different non-radioisotopic alternative devices and technological or research advances in the field;
- Facilitating increased transparency on the benefits and challenges of conversion or replacement, particularly regarding life-cycle costs and end-of-life management for source-based devices;
- Providing training on non-radioisotopic devices or applications to increase the capacity of users to make the transition;
- Funding outreach and educational initiatives that target the next generation of users;
- Evaluating areas where further research or policy efforts are needed and supporting efforts to disseminate that information to the necessary stakeholders; and
- Creating forums for additional discussion and outreach to the user and policymaking communities and build bridges between participants.

Research and Development Approach

Across several agencies, the Federal Government is responsible for supporting research and development utilizing both source-based and non-radioisotopic devices. This research often relates directly to the development of new technology or device components and could promote bringing new, innovative, and competitive non-radioisotopic devices to the market. In addition, there are government agencies that support research related to the use of, or consequence management of, high-activity

³⁴ Miles Pomper, Egle Murauskaite, and Tom Coppen, "Promoting Alternatives to High-Risk Radiological Sources: The Case of Cesium Chloride in Blood Irradiation," Occasional Paper No. 19, page 27.

³⁵ Autorité de Sûreté Nucléaire, "Nuclear Safety and Radiation Protection in France in 2012," <http://www.french-nuclear-safety.fr/Information/Publications/ASN-s-annual-reports/Nuclear-safety-and-radiation-protection-in-France-in-2012>.

³⁶ <http://www.nss2016.org/s/National-Statement-France-f42j.pdf>

³⁷ Canadian Nuclear Safety Commission, Licensing Process: Financial Guarantees, <http://nuclearsafety.gc.ca/eng/nuclear-substances/licensing-nuclear-substances-and-radiation-devices/licensing-process/financial-guarantees/index.cfm>

radioactive sources. These agencies may also play a role in the transition to alternative technology. For example, some policies may include:

- Providing information to support the conversion of existing research data using radioactive sources to non-radioisotopic alternatives,
- Supporting the research and development of non-radioisotopic alternative devices and sharing information about their updates where possible,
- Publicizing emerging innovations as they become viable, via open-source Web site or data centers,
- Sharing information on any existing R&D utilizing source-based device and evaluating whether the research may support a transition to alternative technology, and
- Verifying information of alternative sources whereby developers and end-users could collaborate in the test of the technology and device performance parameters for the intended application.

As a further example, the NNSA Office of Defense Nuclear Nonproliferation (DNN) Research and Development has found that the most effective R&D to promote alternative technologies is relatively high in technology readiness level (TRL) and that smaller companies funded through Small Business Innovative Research (SBIR) grants have been particularly effective in conducting this high-TRL work. The U.S. SBIR program supports scientific excellence and technological innovation through the investment of Federal research funds in domestic small business projects supporting critical American priorities. Currently, nearly all of the projects funded by DNN R&D in support of the alternative technology mission are part of the SBIR program.

Considerations for Government Involvement

When evaluating policy mechanisms to facilitate Federal leadership in promoting non-radioisotopic alternative technology, Federal departments and agencies will need to consider several factors before moving forward.

It will be important for each organization to consider both Federal and agency-specific procurement regulations when implementing a program utilizing a category 1 or 2 source for medical applications. Whether an agency is directly procuring the device or providing grants or incentives toward the procurement, there may be general best practices to promote the consideration and adoption of an alternative device. For example, it may be possible for a Federal agency to require a grant applicant to consider an alternative technology-based device in the future. Other considerations on the procurement side include ownership of custodian responsibilities, such as warranty and maintenance, any liabilities where applicable, and end-of-life management.

Departments and agencies will need to compare existing programs and expenditures on safety, security, and disposition of high-activity radioactive sources against alternative technology measures that might have an impact on total life-cycle costs. Ultimately, agencies will have to balance their specific equities with the national security motivation of facilitating non-radioisotopic alternative technology. In many cases, it may be possible to prioritize permanent risk reduction, but it must be a coordinated effort among all stakeholders. This applies particularly to existing consumers and collaborators within U.S. Government and government-sponsored programs with either high-activity radioactive sources or the non-radioisotopic technology.

Because from a CMS perspective, reimbursement for a procedure that uses a non-radioisotopic alternative device poses no problem as long as the procedure has proper clearance (e.g., from FDA). In general, the topics in this document are support services (i.e., medical sterilization), not direct services, further reducing the likelihood of any impact associated with reimbursement for a procedure. Early adopters of an alternative technology would have to cover any additional costs associated with the activity over and above the reimbursement for the same activity using radioactive source technology.

The FDA makes recommendations to CMS on Investigational Device Exemptions, regarding whether a device is research-related or not. The Center for Devices and Radiological Health (CDRH) clears blood irradiators through the FDA, and the Center for Biologics Evaluation and Research (CBER) clears sterilization irradiators. Blood irradiation pre-dates the medical device regulations of 1976. The CBER and CDRH rely on a guidance document for issues regarding blood irradiation such as recommended dosages. This guidance refers to X-ray and gamma irradiation, but does not apply to ultraviolet (UV) technologies. The CDRH would need to clear UV devices for blood irradiation and blood irradiation use would need a consultation from the CBER.

Case Study: EPA's Alternative Technology Initiative (ATI), 2001–2011

The EPA's initial decision to pursue alternatives was in 2001 out of concern with potential impacts on human health and the environment caused by improper end-of-life management of the devices. A survey of a wide array of stakeholders, including State and Federal Government representatives, manufacturers, trade associations, environmental groups, technical experts and end users, assessed if a potential existed for the successful promotion of alternatives of non-nuclear technologies in the industrial sector. Although industrial, medical, and research sectors use sealed radioactive sources, the focus of ATI was industrial because their small size and portability make them potentially vulnerable to theft or misuse when not adequately secured.

Initial stakeholder research revealed demand for alternative non-nuclear substitutes in many industrial applications because of licensing bureaucracy, potential worker safety issues, training requirements, and security threats. However, the robustness and versatility of current nuclear devices established a high set of criteria for alternatives to meet.

Research showed that alternatives were specific to their intended application, so an alternative might be suitable for only one application, unlike with nuclear, which could be applicable to a wide range of applications. Approval and verification or validation from an appropriate authoritative body was essential to end users for acceptance of alternatives. Research of industry users, alternative manufacturers, research institutions, and trade associations revealed that efforts were isolated and lacked communication between parties essential to the development and successful deployment, adaptation of alternatives. In addition, some alternatives were sporadic and lacked continuity, demand, and follow through.

Among lessons learned, in general EPA found alternative technologies welcomed by user stakeholders for a variety of reasons including the elimination of red tape associated with licensing, training, worker safety and disposition issues. User stakeholders recognized the value verification/validation of alternatives by appropriate authoritative bodies. Concerns with alternatives were very application-specific, and large gaps existed between manufacturers and research institutions developing alternatives, users, and other stakeholders. Integration of technical activities needed to coordinate with all stakeholders to identify and overcome barriers to implementation and synchronization efforts for positive long-term consequences.

The Federal Government has implemented programs in the past to assist in the transition to alternative technologies across a variety of different application areas. Best practices can be gleaned from those programs, which have proven successful in facilitating the transition through procurement, regulations, outreach, or R&D activities. The case study above describes an EPA program, which was successful in hastening the implementation of commercial-ready environmental technologies. Approaches used in the EPA program, like conducting credible and objective verification and analysis of the technology's performance, map well to recommendations listed in Table 3, such as "Support increased information-sharing on non-radioisotopic technologies and related methods." Successful policy approaches are worthy of special consideration by the Federal Government as a potential best practice in the transition to alternative technologies from traditional radionuclide-based technologies.

Chapter 5: Potential Developments in Sealed Source Disposal that Could Affect Alternative Technology

This chapter provides an overview of potential developments beyond those related to the effectiveness of alternative technologies that could have an impact on the adoption and use of non-radioisotopic alternative technologies.

As noted in “The 2014 Radiation Source Protection and Security Task Force Report” there has been significant movement in addressing sealed source disposal challenges in recent years. Those challenges mainly involve availability of disposal options and planning for disposal costs.

Sealed Source Disposal

Commercial disposal options for some sealed sources that are determined to be Class A, B, and C Low-level Radioactive Waste (LLRW) are now available, although disposal challenges remain for certain higher-activity sealed sources.

In addition, certain commercial sealed sources (e.g., certain sources containing Cs-137) that are determined to be waste could be classified as Greater-Than-Class C (GTCC) LLRW. GTCC LLRW has radionuclide concentrations exceeding the limits for Class C LLRW established by the U.S. NRC. NRC or Agreement State licensees generate GTCC LLRW. Sealed sources are one type of GTCC LLRW. There is currently no disposal path for GTCC LLRW. Section 3(b)(1)(D) of the Low-Level Radioactive Waste Policy Amendments Act of 1985 (Public Law 99-240, as amended) specifies that the Federal Government is responsible for the disposal of GTCC LLRW. DOE is the Federal agency responsible for GTCC LLRW disposal. Within DOE, the Office of Environmental Management is responsible for GTCC LLRW disposal. In February 2016, DOE publicly issued the *Final Environmental Impact Statement for the Disposal of Greater-Than-Class C (GTCC) Low-Level Radioactive Waste and GTCC-Like Waste* (DOE/EIS-0375)(Final EIS) to evaluate the potential environmental impacts associated with the proposed development, operation, and long-term management of a disposal facility or facilities for GTCC LLRW and GTCC-like waste.

The Energy Policy Act of 2005 (Public Law 109-58) requires that, prior to making a final decision on the disposal alternative or alternatives to implement, DOE must first submit a report to Congress that describes the alternatives under consideration and other information, including options for ensuring that the generators of GTCC LLRW bear all reasonable costs of disposal. DOE must then await congressional action. DOE is currently developing its report to Congress.

The potential for expanded sealed source disposition options, particularly if the costs of disposition are high, may influence users’ decisions to transition to use of alternative technologies.

Financial Assurance

As disposition options expand, a requirement for financial assurances could reinforce the responsibility of sealed source licensees to put aside funding for the cost of disposal when purchasing a sealed source, and to commercially dispose of their sealed sources when such disposal is available. Moreover, by instituting a regulatory requirement for licensees to provide financial assurances for sealed source disposition costs upfront, licensees could view the requirement as an incentive to transition to alternative technologies (i.e., devices that do not contain radioactive sealed sources) and thereby

increase the production of viable non-radioisotopic alternative technologies. The incentive could be significant if the costs of sealed source disposition are high.

NRC regulations addressing financial assurance for facility decommissioning do not require financial assurance for many byproduct materials licensees using category 1 and 2 sealed sources. The costs associated with disposal or management of high-activity sources that are no longer used can be significant, and can pose a challenge for licensees who have not planned for such costs. In 2015, NRC initiated a scoping study to determine if financial planning requirements for decommissioning and end-of-life management for some radioactive byproduct material, particularly category 1 and 2 sealed sources, are necessary. The NRC provided the results of this scoping study in SECY-16-0046, which included a preliminary staff recommendation to expand financial assurance requirements to all category 1 and 2 byproduct material sealed sources. Staff will proffer a rulemaking plan to the Commission by the end of FY16 to provide the Commission the information necessary to determine whether to pursue rulemaking to expand its financial assurance requirements.

Moreover, the DOE National Nuclear Security Administration (NNSA) operates the Off-Site Source Recovery Project for certain sealed sources of concern to recover excess, unwanted, abandoned, or orphaned sealed sources that pose a potential risk to public health and safety or national security. Financial assurance requirements that help to ensure commercial sealed source licensees are prepared for the cost of disposing of their sealed sources using available disposition options could result in fewer sources meeting the OSRP's recovery criteria. That, along with the potentially high costs of sealed source disposal, could potentially alter users' cost benefit calculations between source based devices and viable alternative technologies.

Conclusion

Issues related to sealed source disposal may not come to a quick resolution; however, there have been steps taken to increase disposal access for some sealed sources. The Federal Government continues to support the development of new and expanded disposal options as well as the consideration of financial assurances to facilitate sealed source management and disposal, particularly for category 1 and 2 sealed sources. Expanded commercial disposition options coupled with regulatory drivers requiring licensees to plan financially for disposition could potentially alter the users' cost benefit calculations between source based devices and viable alternative technologies.

Chapter 6: Best Practices to Facilitate a Transition to Alternative Technologies

This chapter presents recommendations that will facilitate the transition to alternative technologies in the four medical application areas of radiotherapy, medical instrument sterilization, blood irradiation, and research irradiation (Table 3). The recommendations identified fall into four categories and are meant to inform Federal agencies that are developing a strategy to transition to non-radioactive source technologies or applications. The recommendations identified in the table are meant to represent a range of possible actions, and may not be applicable to or feasible for all departments and agencies. In addition, GARS members drew the following five conclusions from this effort:

- Federal departments and agencies should promote adoption of alternative technologies in federally funded programs and facilities by encouraging voluntary incentives, dedicated funding, and facilitated conversion.
- Federal departments and agencies should involve all key stakeholders in adoption of alternative non-radioisotopic technologies and should recognize the role of manufacturers, distributors, and others to develop a sustainable system for managing radioactive devices.
- When comparing technologies, Federal departments and agencies should consider the full life-cycle costs of high-activity radioactive sealed sources, including costs of security, disposition, and potential liability.
- Federal departments and agencies pursuing alternative technology replacements must balance the respective operational and technical needs of the user communities and device stakeholders with national security.
- Users, in compliance with Federal safety and physical security requirements for use of category 1 and 2 radioactive sealed sources in medical applications, are likely to continue using these sources for a considerable time, especially if non-radioisotopic alternatives are not suitable for their purposes.

The recommendations listed in Table 3 identify key opportunities for Federal departments and agencies to take steps that will facilitate the transition to non-radioisotopic technologies where appropriate. The recommendations are general and may not be applicable for all departments and agencies. Identifying and sharing case studies that implement the recommendations in this document, as well as strategies not yet identified, will be important to evaluating the effectiveness and challenges associated with recommendations described. GARS encourages the Federal interagency to continue to share best practices and updates regarding the adoption of alternative technologies.

Federal Procurement or Grant-Making

This category of recommendations identifies options related to the use of government funds for radionuclide-based devices to encourage replacements. These recommendations are most relevant to Federal agencies that have a role in the direct procurement of devices for Federal ownership or usage, or in the grant-making process for procurement and distribution of devices for intramural or extramural research purposes.

The Federal Government should facilitate solicitations for specific alternatives, encourage demonstration of existing alternatives to verify performance, and fund further development of viable

technologies. Additionally, Federal agencies, where appropriate, should work closely with a panel of technology experts including the American National Standards Institute, trade associations, and other groups to develop user-specific requirements and standards.

Agency Priorities

These recommendations identify options related to the institutionalization of policy and certification of replacement devices to make alternative technologies more appealing and to encourage improvements in voluntary replacement technologies. Recommendations in this category are most relevant to Federal departments and agencies that have a key role in promoting information-sharing about both the phase-out of isotopic device(s) and the emergence of non-radioisotopic alternatives. These departments and agencies should consider, where relevant and appropriate, policies and programmatic goals designed to influence discontinued ownership of a source-based device. Furthermore, agencies should collaborate in setting up a “shared open-source database” for the dissemination of information related to alternative technologies, and they should encourage national and global adoption of non-radionuclide-based technologies.

Education and Outreach

The recommendations in this category identify options related to the use of educational or outreach efforts to demonstrate cooperation and collaboration through leading by example in the user community. Recommendations include creating opportunities for training on non-radioisotopic devices and forums for discussion on technological or research advances in the field of alternative technologies.

Research and Development

Recommendations related to the use of research and development grants and publicly funded testing include the creation of a national user facility (e.g., research irradiation test bed facility) to encourage improvements in replacement technologies and encourage the verification/validation and comparison of replacement technologies to traditional radionuclide-based technologies. Recommendations in this category are most relevant for government agencies that can support research and development use of both source-based and non-radioisotopic devices.

Table 3. Summary of Recommendations Relevant to Federal Departments and Agencies

Approach	Recommendations
<p>Federal Procurement or Grant-Making</p>	<ul style="list-style-type: none"> • Federal agencies should look for opportunities where possible to lead by example on the utilization and promotion of alternative non-radioisotopic technologies • Agencies supporting the procurement of devices using high-activity sources or the production of high-activity material for such devices should evaluate whether a need to justify the benefits of those devices relative to those of an alternative technology-based device should be incorporated into their internal policies and procedures • In cases where devices using high-activity sealed sources are favored, the supporting agency should ensure that end-of-life management plans are in place to cover costs associated with source disposition

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<p>Agency Priorities</p>	<ul style="list-style-type: none"> • Agencies should continue to incentivize transitions to alternative technologies by supporting source disposition, such as the Off Site Source Recovery Program, and providing financial incentives for device replacements • Agencies should expedite, where possible, approvals of new non-radioisotopic devices • Agencies should identify opportunities to ease product validation costs for non-radioisotopic medical devices
<p>Education and Outreach</p>	<ul style="list-style-type: none"> • Agencies should support increased information-sharing on related applications and standards for non-radioisotopic technologies • Government should continue to engage stakeholder communities and interagency partners to ensure that policies and programs aimed at facilitating a transition to non-radioisotopic alternatives is done in a manner that supports the requirements of the user communities • Agencies should communicate and coordinate R&D efforts with the user community to facilitate a transition to non-radioisotopic technologies, where possible • Agencies should support opportunities to provide training and education on the operation and development of non-radioisotopic technologies, particularly for rising or next-generation users
<p>Research and Development</p>	<ul style="list-style-type: none"> • Agencies should sponsor independent technical verification studies from a trusted/verifiable source on alternative non-radioisotopic technologies to better understand reliability, reproducibility, operation costs, and comparability • Agencies should continue to invest in primary, applied, and comparative R&D and analytical studies in order to expand and improve the commercial availability of alternative non-radioisotopic technologies

Appendix 1: National Institutes of Health (NIH) and Centers for Disease Control and Prevention (CDC) Survey Results

An informal survey at NIH of 25 current users of Cs-137 irradiators and at CDC of nine current users of Co-60 irradiators yielded the results in Table 4.

Table 4. Results of NIH and CDC Irradiator User Survey

What do you irradiate?	In what volume?	To what dose?	Thoughts on switching from cesium to X-ray?
Mammalian cells	One 6-well plate (12 mL) or up to eight 15-cm dishes (200 mL)	10 Gy	Replacement of the Cs irradiator before we finish our manuscripts would be very bad.
Feeder cells	15- to 50-mL conical tube	40–100 Gy	I don't think it's a problem.
Splenocytes	50-mL tube	20 Gy	It would affect the result and I would have to repeat the experiments.
Human hematopoietic cells for induction of DNA damage	15-mL tube	2 Gy	Experiments would require re-optimization.
Using radiation as a conditioning regimen in mice	Up to 30 mice	2.8 Gy	Experiments would require re-optimization.
Adherent cells	10 plates (60 mm)	DNA damage and senescence	It would not be a problem.
Mouse cells, both MEFs and B-cells	2–5 mL either in tubes or in 6-well plates	2–10 Gy	Research would be terribly compromised. I don't think both sources would produce the same type of lesions.
Feeder cells; Mouse chimera	1–12 96-well plates; 2–60 mice each time	3–50 Gy for feeder cells; 5, 6.5, or 11 Gy for mice	No easy answer unless an experiment is performed directly comparing the two types on any specific experiment.
Feeder cells	30–50 mL	30 Gy	As long as the dose is the same, it would be okay.
Antigen-presenting cells, feeder cells, Mueller cells	5–10 mL	30–80 Gy	It would not be a problem; we would not have to repeat past experiments.
Tumor cells	Cell pellets in 15-mL conical tubes	50–100 Gy	I prefer using a non-radioisotope irradiator.
Feeder cells; Mouse chimera	20- to 30-mL tube; 20 mice	6 Gy 9 Gy	All our mouse experiments were performed using Cs irradiator over the last 10 years; we certainly do not want to change this.
Lymphoid cells to be used as antigen-presenting cells	5–15 mL	30 Gy	A switch to X-ray would be a problem for my research.

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What do you irradiate?	In what volume?	To what dose?	Thoughts on switching from cesium to X-ray?
Human peripheral blood lymphocytes to use as feeder cells in the manufacture of cell-based therapies for patients enrolled in clinical trials	Volume of cells is 50–100 mL	40 Gy	The clinical trials would be compromised if we had to switch as we would most likely have to irradiate in batches.
Feeder cells, tumor cells, and immortalized cell lines	~few hundred μ L to 50 mL	40 Gy for feeder cells; 100–300 Gy for tumor cells or immortalized cell lines	Would have to conduct a few experiments to determine if cells irradiated with X-rays were comparable to those irradiated with cesium.
Feeder cells to determine radiotherapy effects of cancer cell lines	5E6–100E6 cells in 10 mL of media in a 50 mL tube	20 Gy for feeder cells; Up to 100 Gy for radiotherapy experiments	No difference for me.
Chimeric mice	5–25 mice at a time	9.5 Gy	I always thought it would be way nicer to use the X-ray irradiator. Assuming it generates the chimeric animals that we need, there's no reason we couldn't use one.
Human cell lines in culture, c. elegans, yeast cells in culture	From one 5-cm tissue culture dish (1 mL media) to 8 x 20 cm dishes (20 mL each)	10–20 Gy for human cells; up to 200 Gy for c. elegans and yeast cells	We are a DNA repair lab; we would need to confirm the DNA repair response to the same dose is the same for both systems. This would take a long time and would need to be confirmed in a variety of cell types to make sure the switch could be made. Yeast and c. elegans require high dosage, which we do for 100–200 minutes at a little less than 100 rad/min. Some X-ray irradiators have a maximum time of 9999 seconds which is very close to the max exposure we have needed; this is problematic. Also uncertain of maintenance cost compared to a Cs irradiator, and what is its life expectancy? Who pays for all of this? If one is rented for us, people might be willing to try it out, but I am not sure people will want to switch to one without some time to try one out and compare.
Feeder cells and mouse chimera	2- to 4 50-mL tubes; 20–40 mice at a time	100 Gy for cells; 3.5 Gy for mice	X-ray would work for my experiments but I'd have to re-optimize the dose.
Cells in culture to study DNA damage-induced responses	Cells are in 6-well plates; usually 1–2 plates per experiment	2 Gy, 5 Gy, or 10 Gy	I don't think it's a problem since I'm essentially irradiating a monolayer.
Purified Leishmania metacyclic stage parasites; using the irradiated parasites to produce antibodies	Typically 1 mL	300 Gy	It is something we would have to test; not sure if there would be a difference.

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What do you irradiate?	In what volume?	To what dose?	Thoughts on switching from cesium to X-ray?
Mouse chimera	2–20 mice at a time	4.25 Gy	For our experiments, X-ray won't substitute for the Cs irradiator because we use total body irradiation for clinical conditioning.
Mouse chimera (myeloablation to do mouse bone marrow transplant)	5–30 mice at a time	5–10 Gy	As long as the radiation dose is exactly the same, there should be no difference.
Feeder cells; Human foreskin keratinocytes to analyze cellular DNA damage and repair pathways	50 mL tubes, or various sized cell culture dishes (10 cm, 6 wells, 12 wells)	60 Gy for feeder cells 5–10 Gy for DNA damage experiments	I don't see it making much of a difference. But reproducibility of research findings are bound by consistencies in use of major equipment; therefore this would need to be tested empirically.
Mouse chimeras	10–20 mice at a time	9 Gy	It might be safer to use an X-ray irradiator.
Biological specimens	20 vials of 1 mL or 10 vials of 15 mL	5k Gy	Would reduce health concerns of Cs-137 irradiators, may be easier to use/set-up, faster.
Biological specimens/agents	1.5-50mL	20-100 kGy	Not a problem as long as it can inactivate.
Biological specimen/viruses inactivation	50 mL in 50 1.5 mL tubes	5 kGy	Shorter irradiation time with Cobalt. Need to validate new procedure and have biosafety committee meeting.
Inactivation of samples.	10–40 2-mL heat-seal bags	5 kGy	Chamber cannot be any smaller than current system. X-ray seems "unpractical," irradiations already 1-day long.
Inactivation of cell slurries, lysates, spot slides	Up to 2-L bucket at a time; already restricted by chamber size	20-100 kGy	"Impossible to know" whether it will work, but will require much verification.
Inactivation of biological specimens	1 mL	20-100 kGy	"WE DO NOT AGREE TO SWITCH"
Cells from culture or animal	Variable	5 kGy	"I don't foresee this being feasible for our branch on any level"
Inactivation of cell slurries, lysates, spot slides	Up to 2-L bucket at a time; already restricted by chamber size	5 kGy	"Co-60 has a very long track record and I hate to mess with it."
Inactivation of cell slurries, lysates, spot slides	Up to 2-L bucket at a time; already restricted by chamber size	5 kGy	"Impossible to know" whether it will work, but will require much verification.

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Abbreviations

ATI	Alternative Technology Initiative
Bq	Becquerel
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CDRH	Center for Devices and Radiological Health
CFR	Code of Federal Regulations
cGy	Centigray
CIRP	Cesium Irradiator Replacement Program
CMS	Centers for Medicare and Medicaid Services
Co	Cobalt
Cs	Cesium
DHHS	Department of Health and Human Services
DHS	Department of Homeland Security
DNN	Office of Defense Nuclear Nonproliferation
DOD	Department of Defense
DOE	Department of Energy
EPA	Environmental Protection Agency
EPRC	Electronic Product Radiation Control
FDA	Food and Drug Administration
GARS	Interagency Working Group on Alternatives to High-Activity Radioactive Sources
GTCC	Greater Than Class C
Gy	Gray
HSA	High Specific Activity
IAEA	International Atomic Energy Agency
keV	Kiloelectron Volt
kGy	Kilogray
kVp	Kilo Voltage Peak
LLRW	Low-Level Radioactive Waste
MBq	Megabecquerel
NIH	National Institutes of Health

NIST	National Institute of Standards and Technology
NNSA	National Nuclear Security Administration
NRC	Nuclear Regulatory Commission
NSTC	National Science and Technology Council
NSTS	National Source Tracking System
ORIA	Office of Radiation and Indoor Air
OSRP	Off-Site Source Recovery Project
OSTP	Office of Science and Technology Policy
PAS	Prior Approval Supplement
PRT	Pathogen Reduction Technology
R&D	Research and Development
RBE	Radiobiological Effectiveness
RPD	Radiation Protection Division
SBIR	Small Business Innovative Research
STEM	Science, Technology, Engineering, and Mathematics
TA-GVHD	Transfusion-Assisted Graft Versus Host Disease
TBq	Terabecquerel
TECDOC	Technical Document
TRL	Technology Readiness Level
USDA	United States Department of Agriculture
UV	Ultraviolet
VA	Department of Veterans Affairs
WIPP	Waste Isolation Pilot Plant

