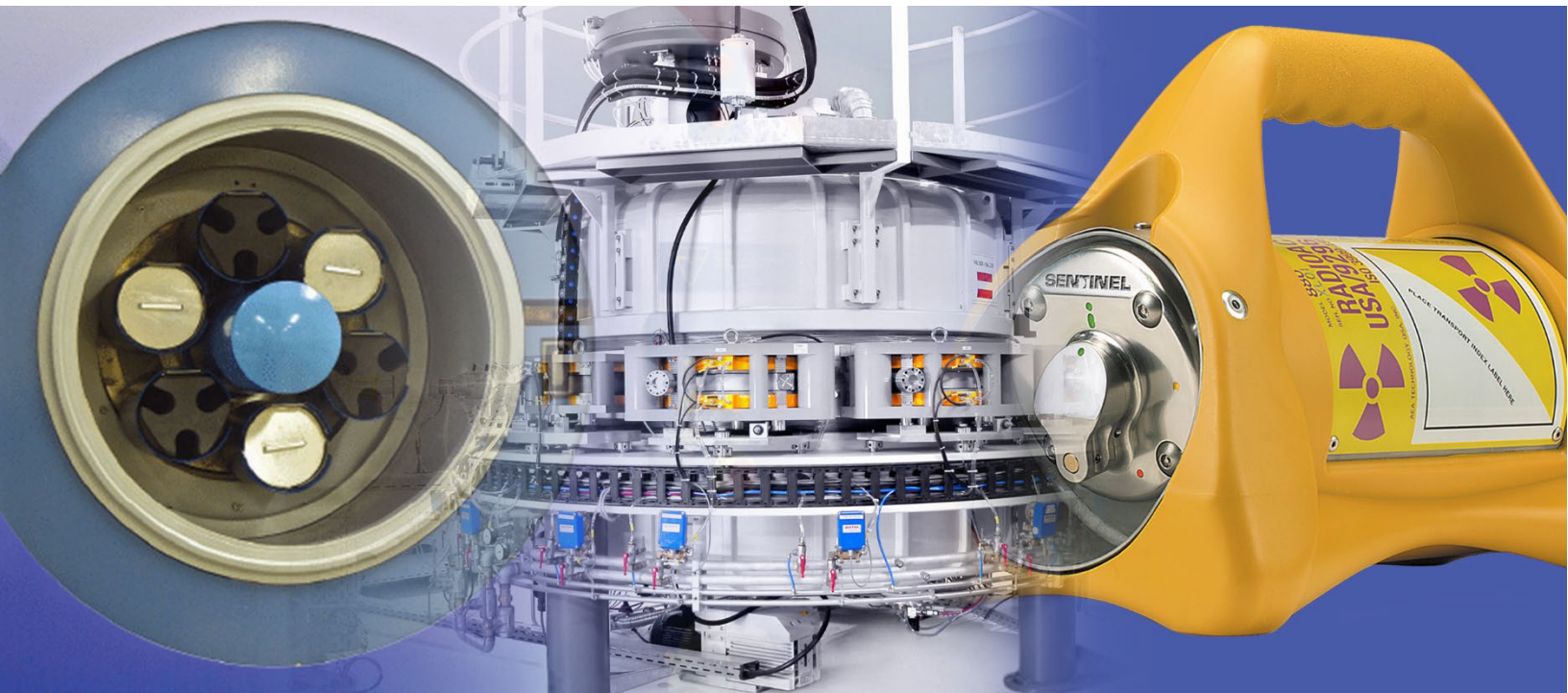




CISA
CYBER+INFRASTRUCTURE



NON-RADIOISOTOPIC ALTERNATIVE TECHNOLOGIES WHITE PAPER

Non-Isotopic Alternative Technologies Working Group

September 2019

U.S. Department of Homeland Security
Cybersecurity and Infrastructure Security Agency

Table of Contents

Executive Summary	1
Introduction and Background	14
Acknowledgements	19
Chapter 1: Alternative Technologies for Blood Irradiation	20
Introduction	20
Commercially Available Blood Irradiation Technology—Isotopic and Alternatives	20
Technology Purchase and Replacement Considerations	24
Chapter 2: Alternative Technologies for Research Irradiation	30
Introduction	30
Commercially Available Research Irradiation Technologies—Isotopic and Alternatives	31
Technology Purchase and Replacement Considerations	34
Chapter 3: Alternative Technologies for Radiotherapy	41
Introduction	41
Commercially Available Radiotherapy Technology—Isotopic and Alternatives	41
Chapter 4: Alternative Technologies for Industrial Sterilization	54
Introduction	54
Commercially Available Industrial Sterilization Technology—Isotopic and Alternatives	55
Technology Purchase and Replacement Considerations	64
Chapter 5: Alternative Technologies for Phytosanitary and Food-Safety Treatments	77
Introduction	77
Phytosanitary and Pathogen Reduction Treatment Options	79
Technology Selection Considerations	87
Chapter 6: Alternative Technologies for Sterile Insect Technique	97
Introduction	97
Sterile Insect Technique Overview	97
Commercially Available Sterile Insect Technique Technology – Isotopic and Alternatives	99
Other Insect Sterilization Techniques	101
Technology Purchase and Replacement Considerations	102
Chapter 7: Alternative Technologies for Well Logging	105
Introduction	105
Overview of Well Logging Science	105
Commercially Available Well Logging Technology – Isotopic Techniques	107

Commercially Available Well Logging Technology — Non-Isotopic Techniques.....	111
Commercially Available Well Logging Technology — Potential Alternative Technologies	114
Technology Purchase and Replacement Considerations.....	119
Chapter 8: Alternative Technologies for Industrial Radiography	125
Introduction	125
Overview	125
Commercially Available Industrial Radiography Technology — Isotopic and Alternatives	125
Technology Purchase and Replacement Considerations.....	131
Appendix 1: Blood Irradiation Devices with FDA 510(k) Classification Status	137
Appendix 2: Lifecycle Cost Estimates for Cesium and X-Ray Irradiators	139
Appendix 3: Glossary	144
Appendix 4: References	147

Executive Summary

This report was developed by the Government Coordinating Council/Sector Coordinating Council (GCC/SCC) Non-Isotopic Alternative Technologies Working Group (ATWG) established under the Critical Infrastructure Partnership Advisory Council (CIPAC).¹ CIPAC supports initiatives to evaluate non-isotopic alternative technologies by fostering public and private sector engagement and identifying gaps in research and development (R&D). The ATWG is co-chaired by representatives from the U.S. Department of Homeland Security (DHS) Cybersecurity and Infrastructure Security Agency (CISA) and the U.S. Department of Energy (DOE) National Nuclear Security Administration (NNSA) Office of Radiological Security (ORS). Its members include representatives from Federal, State, and local government agencies, private sector organizations and companies, and academia.

The counterterrorism intelligence gathered following the September 11th attacks significantly increased concerns related to the security of sealed sources and their potential use in a radiological dispersion device (RDD), which disperses radioactive material over a large area, or a radiation exposure device (RED), which could be hidden in a public area to expose people to radiation. The Energy Policy Act of 2005 (EPAct) established the Interagency Task Force on Radiation Source Protection and Security (Task Force) to evaluate and provide recommendations to the President and Congress relating to the security of radioactive sources in the United States from potential terrorist threats.² The Task Force was required to report any “alternative technologies that may perform some or all of the functions performed by devices or processes that employ radiation sources.” The 2014 and 2018 Task Force reports noted that, while the viability of alternative technologies for some applications has improved significantly, there are still limitations to the widespread implementation of most applications.³

This report describes the status of the development and voluntary adoption of technologies with the potential to effectively replace risk-significant radioactive sources integral to industrial, medical, and research applications.⁴ For each application, the ATWG sought to:

- Examine where commercially available, non-isotopic technologies exist or are under development (including technologies that are commercially available internationally but not yet approved in the United States market).
- Outline the efficacy, lifecycle costs, and applications of these alternative technologies and potential barriers to adoption.

In this report, the ATWG focuses on the current use of the most common Nuclear Regulatory Commission (NRC) Category 1 and 2 sealed sources used in the United States.⁵ These include cobalt-60 (Co-60),

¹ Pursuant to section 871(a) of the Homeland Security Act of 2002 (Pub. L. No. 107–296), the CIPAC structure facilitates the coordination of Federal infrastructure security and resilience programs with the infrastructure security and resilience activities of critical infrastructure (CI) owners and operators in each critical infrastructure sector, as well as State, local, territorial, and tribal governments.

² Energy Policy Act of 2005, Pub. L. 109-58, Sec. 170H.f. August 8, 2005.

³ Radiation Source Protection and Security Task Force, Nuclear Regulatory Commission, *The 2014 Radiation Source Protection and Security Task Force Report*, (Washington, DC, 2014). Available at <http://www.nrc.gov/security/bvproduct/2014-task-force-report.pdf>.

⁴ Category 2 or greater.

⁵ Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material (10 C.F.R. § 37) defines two risk-significant categories of quantities of radioactive material, with Category 1 sources being the most risk-significant.

cesium-137 (Cs-137), iridium-192 (Ir-192), and americium-241 (Am-241) sources in devices used in the following medical, industrial, and research applications:⁶

- Blood irradiation
- Research irradiation
- Radiotherapy
- Industrial sterilization
- Phytosanitary irradiation
- Sterile insect technique
- Well logging
- Radiography

This report was prepared by the ATWG. In drafting this report, the ATWG solicited substantive contributions and comment from subject matter experts on each of the chapters and provided them also to the full ATWG for review. The ATWG also solicited input from the manufacturers and users of devices containing sealed sources and non-isotopic alternative technologies. It is important to note, however, that while this paper reflects a broad Working Group consensus, it does not necessarily reflect, and is not attributed to, any individual member or participant organization.

Technical Summary: Isotopic and Non-Isotopic Radiation Sources

Regardless of radioisotope, radioactive sealed sources are typically composed of radioactive material double-encapsulated in stainless steel by a source manufacturer prior to use in a specific device. These sources continuously produce radiation, but the intensity of the radiation will decrease exponentially with time as dictated by the radioisotope's half-life. The physical size of these sources will depend on the application, but they are generally several inches in length and width. Some radiological devices may use multiple sources; however, cesium-137 and cobalt-60 are the primary radioisotope sources used for the applications addressed in the first six chapters of this report.

The most advanced and commercially viable alternative technologies for these applications are devices that use electricity to produce x-rays or electron beam (e-beam) radiation. X-ray tubes can produce relatively low-energy x-rays up to 500 peak kilovoltage (kVp), while particle accelerators may be used to produce e-beam radiation or high-energy x-rays. Industrial e-beam accelerators range in electron energies from 1 mega-electron volt (MeV) to 20 MeV, although 7.5 MeV to 10 MeV devices are most common for commercial applications. Alternatively, the electrons may be targeted at a dense material such as tungsten to produce bremsstrahlung radiation, which is composed of a broad spectrum of x-ray energies. This spectrum ranges as high as the maximum electron energy used in the accelerator, with the mean x-ray energy being approximately one third of the maximum electron energy. Some accelerators are designed to use both the e-beam and bremsstrahlung x-rays to irradiate targets.

⁶ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008) page 1.

Chapter Summaries

Chapter 1: Blood Irradiation

Blood irradiation is the most common method used in the United States to treat blood prior to transfusion to prevent transfusion-associated graft-versus-host disease (TA-GvHD), a highly fatal disease in which donor lymphocytes—a type of white blood cell—attack host tissues in a recipient patient. This treatment inactivates lymphocytes in blood products for patients susceptible to TA-GvHD. Both ultraviolet (UV) and ionizing irradiation of blood platelets are also used to reduce the risk of pathogens that could cause transfusion-transmitted infections. Hospitals and blood banks treat between 1.5 and 2 million units of blood per year.⁷ Most blood irradiation is accomplished using self-shielded cesium-137 chloride (CsCl) blood irradiator units. Blood irradiation may also be accomplished without radioisotopes with the use of x-ray or UV devices. Both radioisotopic and non-radioisotopic blood treatment devices require Food and Drug Administration (FDA) approval. The FDA requires devices that treat blood with ionizing irradiation to provide a dose of 25 gray (Gy) or greater to the midpoint of the target to meet FDA requirements.⁸

Radioisotope Technology

There are approximately 400 blood irradiators in the United States that use radioactive sources. Nearly all of these devices use cesium-137 (Cs-137) in the form of CsCl.⁹ These devices typically use one or more CsCl sources to expose the target to high doses of gamma radiation. Blood irradiators typically contain 1,000 curies (Ci) or more of CsCl at the time of purchase.

Alternative Technologies

X-ray blood irradiators are currently the only approved replacement technology available for TA-GvHD elimination in the United States. These devices produce radiation using electricity and an x-ray tube to generate electrons aimed at a tungsten or tantalum target. The interaction of the electrons with the target produces x-rays, which irradiate the target chamber. The FDA first approved x-ray blood irradiators in 1999. However, high maintenance costs and significant reliability challenges led to widespread user skepticism regarding the viability of x-ray replacements. In the past several years, technical advances have significantly improved the reliability and operational cost of x-ray irradiators.

The FDA has approved x-ray devices from three manufacturers, which are now commercially available. The FDA also approved two separate UV systems from one manufacturer for blood pathogen reduction in 2014. FDA approval of the systems for red blood cells and whole blood is currently pending.

⁷ Whitaker, Barbee, Srijana Rajbhandary, Andrea Harris, *The 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey Report*, AABB, December 18, 2015, page 63, Available at <https://www.aabb.org/research/hemovigilance/bloodsurvey/Documents/2013-AABB-Blood-Survey-Report.pdf>.

⁸ Ionizing radiation includes not only the gamma radiation produced by radioactive materials, but also the energy produced by x-rays, as well as the higher ultraviolet part of the electromagnetic spectrum. The amount of energy absorbed by matter exposed to ionizing radiation is generally expressed in units of 'gray' (Gy). One centigray (cGy) is equal to one one-hundredth of a single Gy. Exposure of 2500 cGy to the midpoint of a target ensures that no part of the target receives less than the minimum 1500 cGy required for potentially harmful lymphocyte elimination.

⁹ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008) 86; Borchardt, R.W., "Strategy for the Security and Use of Cesium-137 Chloride Sources," Advisory Committee on the Medical Uses of Isotopes (ACMUI) CsCl Irradiator Subcommittee, November 24, 2008, Available at http://hps.org/govtrelations/documents/nrc_cscl-options_secy08-0184.pdf (accessed October 2, 2015); Department of Health and Human Services (HHS), *The 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey Report*, 2015, page 63.

Replacement Considerations

X-ray devices can provide the 25 Gy or greater dose to the midpoint of the target—required by the FDA to be as effective as CsCl sources—and the purchase price of the devices is similar. As a result, technology purchase and replacement decisions largely depend on user confidence in the reliability of currently available x-ray devices and user estimation of the lifecycle costs of the different technologies and the throughput. For example, x-ray irradiators consume electricity and may require a maintenance contract and more frequent maintenance and infrastructure upgrades to provide the necessary power and cooling (both air and water). In some cases, users may opt to purchase more than one x-ray device to account for maintenance downtime. While cesium-137 irradiators are significantly less expensive to operate, they still have associated security requirements. Both cesium-137 irradiators and x-ray units also have procedural and training requirements.

In 2014, DOE/NNSA successfully piloted the Cesium Irradiator Replacement Project (CIRP), which facilitates the voluntary replacement of CsCl and cobalt-60 blood and research irradiators with x-ray devices on a cost-share basis. CIRP support also includes the removal and disposal of the CsCl or cobalt-60 device by NNSA. As of June 2019, 158 blood irradiators have been replaced or are in the process of being replaced through CIRP. This comprises approximately 33 percent of the 2015 United States blood irradiator inventory.

Chapter 2: Research Irradiation

Research irradiators are widely used at hospitals, universities, and governmental and commercial laboratory facilities that conduct radiobiological science and basic, medical, and materials science research. Research irradiators typically expose cellular, small animal, or nonbiological targets to radiation in order to evaluate scientific or medical hypotheses. These studies have different design requirements depending on their purposes. The requirements typically involve four factors, especially when live animal targets are used: percentage depth dose (PDD); dose rate; energy delivery; and the size and type of target.¹⁰ To accurately assess the outcome of a study, researchers must control all four factors within their acceptable margin of error. As a result, these factors are the primary considerations for researchers deciding what type of device to use for an experiment.

Radioisotope Technology

Research irradiators are technologically very similar to blood irradiators. They typically use one or more CsCl or cobalt-60 sources to expose the target to high doses of gamma radiation. However, these devices may accommodate a larger range of target shapes and sizes and enable more precise variation in the dose during exposure compared with blood irradiators. In addition, they often use higher-activity sources. Individual CsCl research irradiators range from under 1,000 Ci to approximately 20,000 Ci, with most devices containing 1,200 to 3,000 Ci. Cobalt-60 models are, on average, higher-activity devices, with some exceeding 30,000 Ci. Approximately 300 gamma research irradiators are in operation in the United States.

Alternative Technology

X-ray research irradiators function in generally the same way as x-ray devices that are used for blood irradiation, using electricity to generate x-rays. The x-rays irradiate the specimen chamber; however, unlike in

¹⁰ PDD is a measure of how the dose varies with depth within a sample. Dose rate is the amount of radiation energy deposited in a target mass in a given amount of time.

the case of radioactive sources, which produce primary gamma rays at just one or a few energies, x-ray devices generate a spectrum of energies below the accelerator maximum energy. As a result, these devices expose their targets to radiation at a wide range of energies.

Research irradiators do not require FDA approval before going to market. Since the 2015 inception of the DOE/NNSA CIRP project, approximately 25 percent of the self-contained research irradiation devices in the United States have been voluntarily replaced or are in the process of being replaced.

Replacement Considerations

Researchers must be able to accurately deliver specific doses of radiation to the target, regardless of depth. Because the PDD capabilities of irradiators depend on the energy spectrum of the radiation delivered, not all devices are able to deliver the required dose to a target with the same efficacy. Due to the differential energy distributions of gamma and x-ray sources, the suitability of x-ray irradiators for medical research currently using cesium-137 or cobalt-60 is highly dependent on specific research goals and requirements. Some research may require a PDD that can only be produced by radioisotope-based irradiators, while a significant number of research areas likely do not. In addition, researchers who are heavily dependent on long-term study protocols or historical data may lack the comparison data necessary to validate their experiment design with an alternate device. While it may occasionally be possible to provide correction factors for moving from a cesium-137 or cobalt-60 irradiator to x-ray devices it must also be possible to accurately assess the resulting uncertainty and support future research needs. These comparison data challenges may discourage or prevent the adoption of alternative technologies in some research applications.

Chapter 3: Radiotherapy

Radiation therapy consists of using radiation to treat cancer and is an essential tool in curative and palliative cancer care. Approximately 60 percent of patients with cancer will receive either external or internal radiotherapy at some point during their treatment. The devices that provide external radiotherapy treatments are typically above the Category 1 threshold, whereas internal radiotherapy devices are smaller and typically below the Category 2 threshold.

External beam radiotherapy, also called teletherapy, is the application of radiation emitted from a device outside of the patient to treat the disease location. Stereotactic Radiosurgery Devices (SRS) are a type of external radiotherapy that precisely target the disease location—particularly tumors of the head or neck—through three-dimensional localization systems from multiple directions. The two types of devices most commonly used for teletherapy and SRS utilize relatively high-energy and high-activity radioactive cobalt-60 sources and linear accelerators (linacs) that generate high-energy x-ray beams. Both technologies use ionizing radiation to destroy tumor cells embedded within the patient.

Radioisotope Technology

Cobalt-60 teletherapy and SRS devices use one or more cobalt-60 sources to deliver the required radiation dose to the patient. These devices typically contain sources with a combined activity 5,000 Ci to 15,000 Ci at the time of purchase.

Alternative Technology

Linacs use high-powered electromagnetic fields to accelerate electrons at a heavy metal target to produce high-energy x-rays that deliver the required dose of therapy to a patient. These devices are also called “e-beam accelerators” or “e-beam.”

Replacement Considerations

Cancer treatment decisions made by physicians and their patients are highly complex and must focus on the health and well-being of the patient. As a result, transition support policies and programs can most likely be applied more effectively to the applications addressed in other chapters of this report. However, for standard teletherapy, medical practitioners generally consider linac devices to be superior to cobalt-60 devices for many types of treatment.¹¹ Linacs produce higher energy photon radiation than cobalt-60, making them particularly effective for the treatment of deep-seated tumors. In addition, linac beam radiation generally has a more uniform dose profile compared with that produced by cobalt-60 devices, enabling more precise tumor targeting within surrounding healthy tissues.

By contrast, both cobalt-60 and linac radiation sources for SRS retain strong adherents among medical professionals. Device selection primarily depends on the range and type(s) of treatment the purchaser expects to provide, the clinical experience and preferences of the practitioners, and the costs associated with the purchase and use of available options. Linacs have higher operational costs due to power, maintenance, and training requirements; they necessitate more extensive and potentially expensive facility shielding than do gamma devices. Their training and maintenance costs are also higher due to their complexity. However, cobalt-60 devices require an NRC license and implementation of additional security requirements. In addition, due to the short half-life of cobalt-60, the devices must be replenished at least once during the service life of the devices.

Chapter 4: Industrial Sterilization

The FDA requires many healthcare products to be sterilized before they are brought to market. These products include a broad spectrum of single-use medical devices and pharmaceuticals. The processing of single-use medical devices accounts for approximately 80 percent of the industrial irradiation volume undertaken by United States companies on an annual basis. Common single-use medical devices include syringes, surgical gloves, masks, gowns, sutures, medical tubing, sterile solution containers, artificial joints, and other implanted devices. Sterilization services are typically provided on a contract basis at large industrial facilities that treat a wide range of products. However, some very large medical device manufacturers also operate in-house sterilization facilities.

Radioisotope Technology

Industrial scale gamma irradiation facilities use hundreds of thousands to millions of Ci of cobalt-60 to sterilize products. In these facilities, conveyance and handling systems expose packaged products to the unshielded racks of cobalt-60 from multiple directions across several hours to achieve the required dose.

¹¹ Page, Brandi R., Alana D. Hudson, Derek W. Brown, Adam C. Shulman, May Abdel-Wahab, Brandon J. Fisher, and Shilpen Patel, “Cobalt, Linac, or Other: What Is the Best Solution for Radiation Therapy in Developing Countries?” *International Journal of Radiation Oncology, Biology, Physics* 2014, 89(3): 476-480.

There are currently 51 gamma irradiators located at 44 sites within the United States.¹² These facilities annually use an estimated collective 150 million Ci of cobalt-60 to sterilize approximately 200 million cubic feet of product. To maintain throughput capacity despite the short half-life of cobalt-60, these irradiators are typically replenished on an annual basis.

Alternative Technology

The primary sterilization modality is ethylene oxide (EtO), with most of the remainder composed of ionizing radiation technologies such as gamma irradiation. The primary ionizing radiation alternatives to gamma sterilization are x-ray or e-beam technology.¹³ In facilities with these technologies, conveyance and handling systems pass the packaged products through a shielded e-beam or x-ray chamber. The products are exposed to radiation from one or more sides to obtain the required dose. Worldwide, less than 5 percent of disposable medical devices are currently sterilized using e-beam devices.¹⁴ There are only two operational dedicated x-ray sterilization processing facilities, one in the United States and one in Europe.

E-beam radiation generally penetrates packaged products less effectively than the gamma radiation from cobalt-60; however, the current industrial practice is to customize the packaging to meet e-beam specifications. Sterilization-method selection factors often include product density and packaging configuration, but proponents of e-beam radiation argue that products can be processed in smaller batches to account for the radiation penetration differential and that the speed of e-beam processing—with dose application in seconds or minutes—can enable equal or better processing volumes.

Replacement Considerations

The choice of a sterilization method is an essential component of the sterile-product development process and may depend primarily on regulatory factors. FDA approval is significantly faster and less expensive if a device manufacturer can show that a device or product—and assurance of that device or product's sterility after processing—is “substantially equivalent” to a previously cleared “predicate” device or product.¹⁵ Due to the historical predominance of gamma processing for sterility assurance, there is a significant regulatory incentive for sterile product and device manufacturers to also use gamma processing for new products. For existing products, a switch in sterilization technology would require expensive product testing and additional regulatory engagement for revalidation. Without greater certainty regarding significant long-term cost savings as a result of switching to an alternative technology, sterile product manufacturers have little incentive to bear the cost and risk of product revalidation. Cost models developed by proponents of gamma processing and alternative technologies rely on significantly different assumptions, making their conclusions difficult to compare.

¹² Gamma Industry Processing Alliance (GIPA), “Cobalt-60 Irradiation and Alternative Technologies,” Presentation to the Alternative Technology Working Group (2015).

¹³ While ethylene oxide (EtO) is used to sterilize a significant volume of products that are incompatible with radiation processing/processes, it is not generally considered an attractive alternative due primarily to environmental and safety factors.

¹⁴ Gamma Industry Processing Alliance (GIPA), *A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products*, White Paper, November, 2017, <http://iiaglobal.com/wp-content/uploads/2018/01/White-Paper-Comparison-Gamma-Eb-Xray-and-EO-for-Sterilisation.pdf>; A reference breaking down the market share by sterilization technique in the United States was not available at publication.

¹⁵ U.S. Food and Drug Administration (FDA), “The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]: Guidance for Industry and Food and Drug Administration Staff,” July 28, 2014, Available at www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM284443.pdf.

Chapter 5: Phytosanitary and Food Safety Applications

Phytosanitary measures applied to food products are used to prevent the spread of invasive pests that may result from the transport of these products between regions. Pathogen reduction treatment of foods and spices help to ensure their safety for consumption. The FDA has determined that gamma, x-ray, and e-beam are equally safe and effective for approved food irradiation treatments, including both pathogen reduction and phytosanitary applications.¹⁶ The most prominent international food safety standards also consider all three radiation sources to be equally safe and effective for approved treatments.¹⁷

A primary challenge of using radiation as a phytosanitary treatment is applying a uniform dose that falls between the regulatory minimum (typically 150 Gy to 400 Gy) and the regulatory maximum (1,000 Gy). As a result, a key measure for these applications is the dose uniformity ratio (DUR) achieved during processing. The DUR expresses the difference between the minimum and maximum dose applied within the targeted product. Dose distributions will vary depending upon the radiation source, the technology and processing configuration, and the physical characteristics of the target. For phytosanitary applications, a DUR at or below 2 is generally required. For pathogen reduction treatments, higher maximum allowed doses make an acceptable DUR for these applications easier to achieve.

Radioisotope Technology

Phytosanitary and pathogen reduction treatment of foods and spices using gamma radiation may take place at the same industrial-scale irradiation facilities that sterilize consumer products and medical devices on a contract basis. Most of these facilities use a million or more Ci of cobalt-60. Although food products are relatively bulky and dense, gamma irradiation can be used to treat relatively large loads of packaged product and still obtain a sufficiently uniform dose, typically with a DUR of 1.6.

Alternative Technologies

FDA rules permit food treatments using x-ray radiation up to 7.5 MeV.¹⁸ The penetration of x-rays and cobalt-60 gamma rays into targeted products is similar, although the higher energy photons generated by a 5 MeV to 7.5 MeV x-ray device will result in an even more uniform dose distribution relative to the 1.25 MeV average energy generated by cobalt-60.¹⁹ Commercial arrangements using x-rays and loads narrower than the dimensions of a standard pallet have achieved DUR under 1.3.²⁰ However, there is currently only one industrial-scale x-ray facility operating in the United States: a Hawaii facility used exclusively for phytosanitary treatment of fresh produce.

FDA rules permit food treatments using e-beam radiation up to 10 MeV. The U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA-APHIS) has certified two e-beam facilities for phytosanitary treatment in the United States. Both are multipurpose service centers that irradiate a variety of consumer products, including food. However, in contrast to the photon energy generated by both gamma

¹⁶ While chemical and extreme temperature treatments are sometimes used for pathogen reduction or phytosanitation, they are not generally considered to be attractive alternatives for products amendable to treatment with radiation gamma or non-isotopic sources.

¹⁷ Codex Alimentarius, "General Standard for Irradiated Foods," Codex Stan 106-1983, Rev. 1-2003.

¹⁸ FDA rules allow x-ray radiation to up to 7.5 MeV when tantalum or gold is used as the electron beam target in the device, which is nearly always the case. If alternative target materials are used in the device, the rules maintain a 5 MeV limit on x-ray applications. See 21 C.F.R. § 179(B): Radiation and Radiation Sources.

¹⁹ International Atomic Energy Agency, "Manual of Good Practice in Food Irradiation," Technical Reports Series No. 481 (2015).

²⁰ Hallman, Guy J., "Phytosanitary Applications of Irradiation," *Comprehensive Reviews in Food Science and Food Safety*, 2011, 10; Guy J. Hallman and Carl M. Blackburn, "Phytosanitary Irradiation," *Foods*, 2016, 5, 8; doi:10.3390/foods5010008.

sources and x-ray technologies, e-beam radiation has a relatively short range and less ability to penetrate targeted products. As a result, the size and density distribution of the processing containers and targeted products are particularly important considerations for achieving the required dose with an acceptable DUR.

Replacement Considerations

Technical feasibility and processing costs are the primary factors for United States food producers in choosing between e-beam and gamma processing. For example, to compensate for the reduced penetration of e-beam radiation, e-beam facilities may use smaller totes for processing. These facilities may also irradiate containers from two opposing sides by flipping or rotating the processing containers for a second exposure or by using two accelerators to irradiate both sides of the product simultaneously. However, these measures can increase the processing time or consumer costs. For gamma processing, facilities must consider the cost to annually replenish the decayed cobalt-60.

There are several additional factors that may impact the selection of an irradiation technology for phytosanitary or food-borne pathogen reduction applications and the incentive of irradiation service providers to make it available. These include the ability of the technology to effectively process a range of packaged and unpackaged products that may have significantly different dosage and DUR requirements while maintaining consistent and sufficient throughput. The throughput of a facility is largely driven by peak product demands, which may also affect the irradiation time—a key production cost factor.

Chapter 6: Sterile Insect Technique

The sterile insect technique (SIT) is a type of pest control used to suppress or eradicate a harmful insect pest species, such as one that damages agriculture or causes disease in humans, in a given region. SIT involves the use of radiation to reproductively sterilize large volumes of the male insects of the harmful species (or their larvae). The sterilized males are then released into the targeted area to mate with the indigenous, non-sterilized female insect population. Because no offspring are produced, the result is a suppression of the harmful pest population. The repeated introduction of sterile male insects across many reproductive cycles can result in control or local eradication of the harmful pest species and reduce its negative societal impacts (e.g., agriculture destruction, disease) to a tolerable level.

Exposure to ionizing radiation is the primary means of insect sterilization. This radiation may come from gamma-emitting isotopes such as cesium-137 or cobalt-60, or x-rays, or e-beams. To be effective, the targeted insect volume must be exposed to a dose high enough for sterilization, but not so high that the ability of the insects to mate after release is negatively affected (i.e., a sufficiently low DUR must be achieved).

Radioisotope Technology

Most gamma-based SIT uses self-shielded gamma devices. These devices contain up to 24,000 Ci of cobalt-60 or 12,000 Ci of cesium-137 and are capable of a 40 Gy/min dose rate. SIT may also employ large panoramic cobalt-60 irradiators used for medical device sterilization and phytosanitary applications. Worldwide, there are approximately 24 self-shielded cobalt-60 units and 10 cesium-137 units used for SIT. In addition, there are 18 panoramic cobalt-60 irradiators that may be used for this application.

Alternative Technology

The primary non-isotopic alternative for SIT is irradiation using relatively low-energy x-ray devices (150 to 225 kiloelectronvolt [KeV]). These devices require a reliable high-energy power source and the necessary operation and maintenance expertise. There is one industrial e-beam facility that may be used for SIT applications.

Replacement Considerations

A key consideration for SIT programs in selecting an irradiation technology is the ability to irradiate the necessary insect volumes while maintaining an acceptable DUR. In addition, the irradiator throughput should be sufficiently large to produce enough sterilized insects that each release into the targeted region can noticeably reduce the harmful pest population. The irradiation facility should be near the insect dispersion site when feasible; transportation time and conditions can reduce the survivability of the sterilized insects and diminish their ability to mate with indigenous females after release into the wild. The insects must also be kept in environmental conditions that will not otherwise harm them.

The low-energy x-rays used for SIT typically have a lower dose rate and less effective radiation penetration than cobalt-60 and cesium-137 devices; as a result, their insect throughput is typically lower. In addition, the longer processing times can reduce the useful reproductive lifetime in the wild for the sterilized insects. Despite these constraints, x-ray devices can achieve the DUR and throughput required for an effective SIT program, particularly when advanced filtration designs are used. E-beam facilities, though rarely used, have a high potential processing capacity and an acceptable penetration depth for SIT applications. There are still areas for improvements in the technology; these include balancing the requirements of energy, dose rate, and DUR. Currently, alternative technology options for SIT applications are limited. Furthermore, there is an insufficient market size for SIT to incentivize commercial developers to produce specialized SIT devices.

Chapter 7: Well Logging

Well logging generally refers to the use of a measurement device for the continuous characterization of geological formations along the depth of a well. The most common and economically important use of well logging techniques is the exploration and development of oil and natural gas. For these applications, well loggers typically use several types of tools to collect and interpret data for geologic parameters: density, porosity, lithology, mineralogy, and fluid saturation. Well logging tools must be durable enough to withstand the extremely harsh operational conditions thousands of feet below the surface.

Radioisotope Technology

Radioisotope based-techniques (such as gamma backscatter, neutron backscatter, and neutron capture spectra) are currently used almost exclusively to measure the density, lithology, porosity, and mineralogy of geological formations around a well.²¹ The density and lithology are usually determined using a device with a 1–3 Ci cesium-137 source, significantly below the 27 Ci Category 2 threshold. The cesium-137-based density measure is typically accurate to within ± 0.01 gm/cc in both clean formations and shales. This translates into a porosity accuracy of better than ± 1 porosity unit (pu), which is the most accurate log-based measure of porosity.

²¹ Backscatter is the reflection of subatomic particles or photons at diffuse angles and reduced energies.

Neutron sources, using americium-241 mixed with beryllium (Am-241/Be), are used to determine the lithology and porosity of the formation. The neutrons emitted from the source undergo primarily elastic scattering with hydrogen nuclei in the geologic formation to moderate (i.e., reduce in kinetic energy, or slow down) to thermal energies. The thermalized neutrons then diffuse and are finally absorbed by the surrounding media. These devices use the differential readings of multiple neutron detectors to determine the porosity value. Am-241/Be sources may also be used for mineralogy measurements by taking advantage of thermal neutron capture and characteristic gamma emissions to determine the surrounding earth. Although the radioactivity of these sources varies, many of the Am-241/Be sources used in well logging applications are 16.2 Ci, with some older sources above the Category 2 threshold, or aggregated by licensees into Category 2 quantities.

Alternative Technology

The neutrons and gamma rays used in well logging applications can be produced using electricity and particle accelerators, although such accelerators are not currently developed to the point of widespread commercial viability. The most common electronic neutron source is a D-T neutron generator. In D-T generators, a projectile deuterium (D) particle is accelerated to high speeds against a target foil impregnated with tritium (T), resulting in fusion-generated 14.1 MeV neutrons. However, the porosity sensitivity of D-T neutrons is much lower compared with Am-241/Be sources. Recently, three other neutron generators—deuterium-deuterium (D-D), deuterium-lithium (D-Li7), and a dense plasma-focus accelerator (DPF) that accelerates alpha particles on to a beryllium target—have undergone study for well logging applications. Relative to Am-Be-based generators, D-D generators will be more sensitive to porosity; D-Li7 generators will be similarly sensitive; and DPF generators will be identically sensitive. However, design and operational tradeoffs would be needed to optimize the choice of neutron generators in logging applications.

Acoustic sources may be used for certain petrophysical measurements. This technique allows determination of porosity, lithology, and supply estimates of permeability, fluid identification, and viscosity. However, the resulting relations depend on rocks' mechanical properties, and may not be linear. The accuracy of acoustic porosity is on the order of 2-4 pu. The depth of investigation is several feet from the probe, making it one of the farther-reaching interrogative options for well logging. Under complex geological conditions, acoustic measurements may be able to fill in the gaps left by traditional nuclear measurements.

Nuclear magnetic resonance (NMR) is used in well logging to determine porosity, fluid types, and viscosity. NMR uses two electro-magnets, with the first magnet projecting a powerful magnetic field and the second magnet creating a weaker oscillation in that field. This perturbs and polarizes the hydrogen nuclei within range. There does not need to be any assumption of the rock lithology to determine its porosity. The disadvantage of using NMR technology is that wireline logging is a slow interrogation technique, with NMR tools generating data at about 200 feet per hour, whereas standard logging tools generate similar data at about 1,800 feet per hour.²² Time is a valuable commodity in oil exploration, and the slow speed of alternate technology is a major impediment to widespread use. Neither acoustic nor NMR tools provide mineralogy information.

²² Akkurt, Ridvan, et al., "Towards Everyday-NMR: An Operator's Perspective," *Petrophysics*, 2009, 50 (6): 495-510, SPWLA-2010-v51n3a1.

Replacement Considerations

Well logging is a multi-faceted operation with multiple interrelated and competing requirements. The requirements for well logging devices can vary significantly based on application and can generally be broken down into several broad categories: operating environment, logging speed, density accuracy, porosity error, generator lifetime, interpretation requirements, and traceability to legacy data. In general, non-radioisotopic technologies for these applications are not currently considered to be fully viable replacements for radioisotope-based logging tools; only electronic nuclear source-based tools have that potential.

Nearly 70 percent of the logging units in the United States well logging industry are small- and medium-sized firms. These companies have pricing and equipment utilization pressures, which become even more acute when the price of oil decreases. Due to these pressures, small and mid-sized companies in the energy service industries have little interest or incentive to invest in new technologies. The effective use of alternative technologies and interpretation of the resulting data could also require these companies to invest in extensive training. Furthermore, the data provided by the new technologies may not be directly comparable with data previously collected using radioisotope sources.

Chapter 8: Radiography

Non-destructive testing (NDT) and analysis is a vital tool for industry. It is often necessary to inspect the safety and quality of both solid metal and welded systems—such as pipes, boilers, turbines, and structural supports—to ensure that everything was built to design and operational specifications. A failure of these systems can be severe, with consequences to worker and population safety, the environment, the economy, and the financial health of a project or company.

There are several types of NDT available, including, but not limited to, gamma radiography, x-ray radiography, ultrasonic, eddy current, magnetic particle, and dye penetrant. Gamma radiography is an NDT technique that uses ionizing radiation (comprising mostly gamma rays) from a radioisotope source to perform radiography. X-ray radiography does not use a radioactive source but does use electrically generated ionizing radiation (e.g., x-rays from bremsstrahlung radiation) to perform radiography. Both techniques can be used to find defects beneath the surface of the material.

There are other NDT techniques that do not use radioisotopes, but may use electricity, magnetism, visible light, microwaves, millimeter waves, ultrasound waves, or chemicals to probe materials under test. Each of these techniques has its own advantages and disadvantages. For example, some are best used to find surface-level defects and would not be considered direct suitable replacements for gamma radiography, which can probe deep beneath the surface.

Radioisotope Sources

The most common isotope used in gamma radiography in the United States is iridium-192 (Ir-192), which is found in most handheld gamma radiography cameras. New iridium-192 sources for these devices are typically about 100 Ci. However, due to the very short half-life of iridium-192—just 73.8 days—such sources must be replaced roughly every 6–8 months. Radiography devices that use between 60 Ci and 300 Ci of cobalt-60 are also common. However, these devices are much less mobile than the hand-held radiography cameras due the heavy shielding required for the high-energy material.

Regardless of isotope, in gamma radiography, a gamma-emitting radioisotope source is brought near to one side of the object to be examined. On the other side of the object is a gamma ray detector (e.g., film or storage phosphor plate or direct conversion digital detector plate). Some of the gamma rays will pass

through the object, but, depending on the material thickness and density, some will be attenuated, resulting in variations of gamma intensity detected or interacting with the detector in the two-dimensional space behind the object. Areas with less material (or, more specifically, electron clouds) will absorb or attenuate less and will result in more gamma rays detected in the two-dimensional space behind the object, thereby generating a gray-scale image of the defects within the structure.

Alternative Technology

X-ray systems generate images of defects in an object the same way gamma radiography does, but require an active and reliable power source to function; this is particularly important for uses in the field far from established infrastructure. In a factory or laboratory setting, however, x-ray radiography generally provides superior image quality compared with gamma devices.

Ultrasonic testing (UT) is a common and effective industrial tool for finding defects in materials and welds. Unlike radiography, it only requires access to one side of a material to search for defects. Using this method, a high-frequency sound wave is sent through a transducer and propagated through the material of interest. As the acoustical waves pass through the material, they may be reflected (i.e., echoed) by the free end of the material, defects and larger pores, or a differing medium.

Replacement Considerations

Viable replacement technologies must be able to perform well in extreme environments and remote field locations without ready access to reliable power. Both x-ray units and their remote-power batteries are more sensitive to extreme environments. Gamma radiography is also easier to use in places that are difficult to access, such as those that are spatially limited or high above a surface that would preclude the use of more voluminous or heavy equipment.

Both gamma and x-ray radiography often require the radiographer to establish a radiation “exclusion zone” at the worksite to prevent inadvertent worker exposure to radiation; these zones can interrupt work functions. An operational advantage of UT is that it can generally be applied without significant facility disruption: No radiation exclusion zone is required. The absence of additional safety/security considerations is also an advantage compared with gamma radiography.

UT is currently used primarily as a complimentary technique with radiography NDT. It may be viable as a replacement to gamma radiography in some limited applications.

Introduction and Background

A wide variety of medical, industrial, and research applications in the United States use radioactive sealed sources thousands of times each day.²³ Essential applications including cancer therapy, sterilization of medical devices, irradiation of blood, irradiation of cells and small animals for biomedical research needs, nondestructive testing of structures and industrial equipment, and exploration of geological formations to find oil and gas deposits²⁴ traditionally use sealed sources; however, the concentrated radioactivity and portability of commonly used sealed sources raise some concern that their loss or theft could lead to malicious use.

This paper focuses on potential replacement applications for the most common Category 1 and 2 radioactive sealed sources. The Nuclear Regulatory Commission (NRC) defines two risk-significant categories of quantities of radioactive material, with Category 1 sources being the most risk-significant. The NRC requires licensees that possess aggregated Category 1 or 2 quantities of radioactive material to implement the security requirements of NRC Title 10 of the Code of Federal Regulations (C.F.R.) Part 37, Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material (Part 37) or an equivalent Agreement State regulation, in addition to existing safety, security, and control regulations in other Parts.²⁵ These requirements apply to individual Category 1 and 2 sources as well as to aggregate quantities of these materials.²⁶ For example, although most individual well logging sources containing Americium-241 (Am-241) are below the Category 2 activity threshold, licensees who aggregate multiple sources above the Category 2 threshold are required to implement the security measures described in Part 37. In addition, most radioactive sources or quantities of material below the Category 2 threshold must regardless be secured from unauthorized access or removal while in storage, and licensees must maintain constant control while these sources are in use.

The counterterrorism intelligence gathered following the September 11, 2001 attacks significantly increased concerns related to the security of sealed sources and their potential use in a radiological dispersion device (RDD), which disperses radioactive material over a large area, or a radiation exposure device (RED), which could be hidden in a public area to expose people to radiation. To reduce the risks posed by radioactive sealed sources, the Energy Policy Act of 2005 (EPA) included the importance of developing and implementing “alternative technologies in order to reduce the number of radiation sources in the United States.”

Several federal and international initiatives are analyzing the feasibility of transitioning from radioactive source-based technologies to commercially available alternatives and encouraging the development of new technologies where commercially available alternatives do not exist.

²³ Radioactive material used in these applications is typically sealed in a metal capsule, such as stainless steel, titanium, or platinum, to prevent its dispersal. These capsules are commonly referred to as “sealed sources.”

²⁴ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008).

²⁵ U.S. Nuclear Regulatory Commission, “Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material (10 C.F.R. § 37),” December 2015 (Washington, DC).

²⁶ Aggregated is defined in the regulation as “accessible by the breach of a single physical barrier that would allow access to radioactive material in any form, including any devices that contain the radioactive material, when the total activity equals or exceeds a Category 2 quantity of radioactive material.”

U.S. Prevalence of Radiological Sealed Sources

Approximately 77,000 Category 1 and 2 radiological sealed sources are currently licensed in the United States.²⁷ The most common radioisotopes (by activity) are:

- **Cobalt-60:** This radiation source is mainly used for consumer product and medical device sterilization, scientific and engineering research, and cancer research and therapy applications, as well as in some industrial radiography applications. There are approximately 68,000 Category 1 and 2 sources that account for approximately 90 percent of the total Category 1 and 2 material licensed in the United States.²⁸
- **Cesium-137:** Cesium is the main source used in blood and research irradiation. In well logging, it is employed to measure formation density, which gives the most accurate value of porosity, an important parameter in estimating petroleum reserves. Cesium can exist as an insoluble ceramic or as a soluble pressed powder (cesium-137/chloride, or CsCl). Approximately 3,400 Category 1 and 2 cesium-137 sources are licensed for use in the United States, accounting for more than 4 percent of total licensed Category 1 and 2 sources.²⁹ A ceramic form of cesium is used for well logging sources. Cesium-based well logging sources are typically below the Category 2 threshold, although they may still be aggregated at some user locations into Category 2 quantities of material. The primary cesium-137 gamma emission is at 0.662 MeV (662 keV).
- **Iridium-192:** This metal source is used to conduct nondestructive industrial testing (NDT) that examines the integrity of structures and manufactured components; it is also used to treat localized tumors. The devices that use these NDT sources are typically portable, which make them more vulnerable to theft than large, stationary devices, such as blood and research irradiators. However, these sources have short half-lives (approximately 74 days) and are encapsulated in a form that is not as easily dispersible, if misused.³⁰ With approximately 3,700 Category 2 sources licensed for use in the United States, iridium-192 sources comprise approximately 5 percent of all licensed Category 1 and 2 sources in the country.³¹ The primary iridium-192 gamma emission is at 0.375 MeV (375 keV).
- **Americium-241:** Americium is often mixed with beryllium to produce neutron sources, which are then mainly used to map oil and gas deposits in well logging. It is small, mobile, and used in remote locations, making it a high-risk sealed source. Approximately 200 Category 2 americium-241 sources are licensed for use in the country, accounting for less than 1 percent of total licensed Category 1 and 2 sources in the United States.³²

Domestic Policy on Non-Radiological Alternative Technologies

In 2003, the U.S. Department of Energy (DOE) and the NRC assessed the potential risks posed by radioactive sealed sources commonly used in industry and government and outlined ways to improve sealed source security and protection. Their report—*Radiological Dispersal Devices: An Initial Study to Identify*

²⁷ Statistic provided by the Nuclear Regulatory Commission.

²⁸ Ibid.

²⁹ Ibid.

³⁰ Ibid.

³¹ Ibid.

³² Ibid.

Radioactive Materials of Greatest Concern and Approaches to Their Tracking, Tagging, and Disposition—recommended DOE assess “the feasibility and cost-benefit of using nonradioactive materials instead of radioactive sources.”³³ Congress created the Federal Interagency Radiation Source Protection and Security Task Force (Task Force) in the EPAct. The Task Force was tasked with making recommendations to Congress and the President regarding the security and protection of sealed sources, including any “appropriate regulations and incentives for the replacement of devices and processes” that use Category 1 and 2 sealed sources.³⁴ Congress also directed the NRC to fund a National Academy of Sciences (NAS) study of the commercial uses of high-risk sources and the feasibility of replacing them with lower-risk alternatives.

The NAS study, published in 2008, identified a wide range of industry efforts to develop non-isotopic technologies for applications that typically utilize radiological devices. The report found that while alternatives for americium-241, cesium-137, cobalt-60, and iridium-192 sources do exist, they may not be viable or practical. One finding demonstrated that “neither licensees nor manufacturers now bear the full cost of liabilities related to misuse of Category 1 and 2 radiation sources.” The report recommended the United States government support research and development (R&D) in cases where alternatives were not viable and “adopt policies that provide incentives (market, regulatory, or certification) to facilitate the introduction of replacements.”³⁵

Following the 2008 NAS assessment, the Task Force recommended in a 2010 report that the Federal Government “enhance support of short-term and long-term research and development for alternative technologies” to replace widely used high-risk sources, and “investigate options such as a voluntary prioritized, Government-incentivized program to support adoption of effective alternatives as they become available.”³⁶ The 2014 and 2018 Task Force reports noted that, while the viability of alternative technologies for some applications has improved significantly since the 2008 NAS and 2010 Task Force reports were published, there are still limitations to their widespread implementation for most applications. As a result, the Task Force recommended that the United States government continue to support R&D efforts and to investigate voluntary, incentivized programs to replace radioactive technologies that “meet technical, operational, and cost requirements” when available.³⁷ One of these efforts includes a review of the feasibility of transitioning from radioactive-source-based technologies to commercially available alternatives.

2019 Non-Isotopic Alternative Technologies Working Group Report

The Non-Isotopic Alternative Technologies Working Group (ATWG) was established to conduct a review of the current state of the technology for radioisotope and non-radioisotope technologies. The Government Coordinating Council/Sector Coordinating Council (GCC/SCC) Non-Isotopic ATWG supports initiatives to evaluate alternative technologies by fostering public and private sector engagement, identifying gaps in R&D, and building a path forward to address public and private sector security needs. The ATWG is co-

³³ U.S. Department of Energy (DOE)/U.S. Nuclear Regulatory Commission (NRC) Working Group, *Radiological Dispersal Devices: An Initial Study to Identify Radioactive Materials of Greatest Concern and Approaches to Their Tracking, Tagging, and Disposition*, U.S. Department of Energy and U.S. Nuclear Regulatory Commission, May 2003. Available at <http://energy.gov/sites/prod/files/edg/media/RDDRPTF14MAYa.pdf>.

³⁴ Energy Policy Act of 2005, Pub. L. 109-58, Sec. 170H.f. August 8, 2005.

³⁵ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008) 10.

³⁶ Radiation Source Protection and Security Task Force, Nuclear Regulatory Commission, *The 2010 Radiation Source Protection and Security Task Force Report*, (Washington, DC, 2010), page 4. Available at <http://www.nrc.gov/security/byproduct/2010-task-force-report.pdf>.

³⁷ Ibid.

chaired by representatives from the Department of Homeland Security (DHS) Cybersecurity and Infrastructure Security Agency (CISA) and DOE National Nuclear Security Administration (NNSA). The Working Group was formed under the DHS Critical Infrastructure Partnership Advisory Council (CIPAC).³⁸ Its membership includes representatives from Federal, State, and local government agencies; private sector organizations and companies; and academia, with experts on the use and replacement of high-risk radioactive sealed sources in industry, research, and medicine.

In preparation of this report, DHS facilitated stakeholder engagements and expert presentations on each of the major risk-significant radioactive source applications, including:

- Blood Irradiation
- Research Irradiation
- Radiotherapy
- Industrial Sterilization
- Phytosanitary Irradiation
- Sterile Insect Technique
- Well Logging
- Radiography

The ATWG developed this report to:

- Examine where commercially available, non-isotopic technologies exist or are under development (including technologies that are commercially available internationally but not yet approved in the United States market).
- Outline the efficacy, lifecycle costs, and applications of these alternative technologies and potential barriers to adoption.

This paper focuses on Category 1 and 2 sealed sources used in medical, industrial, and research applications that pose the highest potential security risks to the United States. It includes a chapter on each of these applications. However, development of the report presented the ATWG with certain organizational challenges, particularly regarding inclusion of information on technical, operational, or lifecycle cost factors substantially the same for radioactive sources or non-radioactive replacement technologies relevant to multiple chapters. Although one of the original ATWG goals for this report was for each chapter potentially to stand alone, certain chapters are nevertheless very complementary.

For example, many of the same industrial scale gamma, e-beam, and x-ray irradiation facilities and technologies are currently or potentially used for both the medical device and consumer product sterilization addressed in Chapter 4, as well as for the phytosanitary and food-borne pathogen reduction treatment applications addressed in Chapter 5. As a result, in certain instances, technical or operational information that would apply to the applications discussed in two (or more) chapters is more fully described in one or the other. Similarly, the self-shielded cesium-137 and cobalt-60 irradiators and their potential x-ray replacements addressed in Chapters 1, 2, and 6—which discuss blood irradiation, research irradiation, and sterile insect technique respectively—share many of the same technical and operational features. In other instances, highly similar or identical information appears in multiple chapters, particularly when necessary to technology replacement considerations. For example, certain lifecycle costs apply to nearly all Category 1

³⁸ Pursuant to section 871(a) of the Homeland Security Act of 2002 (Pub. L. No. 107–296), the CIPAC structure facilitates the coordination of Federal infrastructure security and resilience programs with the infrastructure security and resilience activities of critical infrastructure (CI) owners and operators in each critical infrastructure sector, as well as State, local, territorial, and tribal governments.

and 2 sealed sources regardless of application. As a result, some of this information is included in multiple chapters, in some cases using identical language to ensure consistency.

In drafting this report, the ATWG solicited substantive contributions and comment from subject matter experts on each of the chapters and provided them also to the full ATWG for review. The ATWG also solicited input from the manufacturers and users of devices containing sealed sources and non-isotopic alternative technologies. It is important to note, however, that while this paper reflects a broad Working Group consensus, it does not necessarily reflect, and is not attributed to, any individual member or participant organization.

Acknowledgements

White Paper Contributors

Ahmed Badruzzman, PhD, ANS Fellow, Pacific Consultants and Engineers

Alex Bakken, PhD, Niowave Inc.

Chase Boulware, PhD, Niowave Inc.

Antone Brooks, MD

Nelson Chao, MD, Duke University

Philippe Dethier, MEVEX Corporation

Kate Fry, America's Blood Centers

Richard Gonzales, Richblo2d Biologics Consulting Services LLC.

Paul Gray, Gamma Industry Processing Alliance

Amanda Grimm, Niowave Inc.

Jacob Kamen, PhD, Mount Sinai Medical Center

Thomas Kroc, Fermilab

William Lorenzen, Boston Children's Hospital

Andrew Parker, International Atomic Energy Agency

Suresh Pillai, PhD, Texas A&M University

Charles Potter, Sandia National Laboratories

Mark Shilton, QSA Global Inc.

Ruth Sylvester, America's Blood Centers

Cindy Tomlinson, American Society for Radiation Oncology

Stephen J. Wagner, American Red Cross

Paul Wynne, International Irradiation Association

National Nuclear Security Administration

Nick Butler, National Nuclear Security Administration

Lance Garrison, National Nuclear Security Administration

David Martin, Energetics in support of the National Nuclear Security Administration

Malika Taalbi, National Nuclear Security Administration

U.S. Department of Homeland Security

Ryan Bechtel, PE, Cybersecurity and Infrastructure Security Agency

Ulander Gervais, Cybersecurity and Infrastructure Security Agency

Rachel Liang, Cybersecurity and Infrastructure Security Agency

Kate McClaskey, Nexight Group, LLC in support of the Cybersecurity and Infrastructure Security Agency

In drafting this report, the ATWG solicited substantive contributions and comment from subject matter experts, not all of whom are listed above, on each of the chapters and provided them also to the full ATWG for review. The ATWG also solicited input from the manufacturers and users of devices containing sealed sources and non-isotopic alternative technologies. However, it is important to note that this paper reflects a broad Working Group consensus, but does not necessarily reflect, and should not be attributed to, any individual member or participant organization.

Chapter 1: Alternative Technologies for Blood Irradiation

Introduction

Blood irradiation is the most common method used in the United States to inactivate lymphocytes—a type of white blood cell—in blood products for patients susceptible to transfusion-associated graft-versus-host disease (TA-GvHD). TA-GvHD occurs when donor lymphocytes proliferate and attack host tissues in a recipient patient. While rare, TA-GvHD has a fatality rate of more than 90 percent.³⁹ The definition of patients at risk for TA-GvHD may differ from hospital to hospital, and not all patients at risk are correctly identified. To circumvent failure to identify some at-risk patients, some United States hospitals irradiate all blood products for transfusions, not just those for specific patient populations.⁴⁰ According to the AABB (formerly known as the American Association of Blood Banks)—an international, not-for-profit association representing individuals and institutions involved in transfusion medicine—its members irradiate approximately 1.8 million red cell and platelet units per year.⁴¹

Commercially Available Blood Irradiation Technology—Isotopic and Alternatives

Traditional isotopic irradiators expose blood products to ionizing radiation using self-shielded gamma irradiators that contain Category 1 quantities of cesium-137 (Cs-137) in the form of cesium chloride (CsCl), a pressed powder encapsulated in stainless steel. Blood irradiators are mostly housed in hospitals, blood banks, and blood centers—facilities that are generally open to the public, though with controlled access areas.

Non-isotopic x-ray irradiators have emerged as an effective alternative technology to CsCl blood irradiators. In some countries where the devices are governmentally owned, x-ray units have entirely replaced devices using CsCl.⁴² X-ray devices from three manufacturers have been approved by the FDA for TA-GvHD prevention and are now commercially available in the United States.⁴³

Ultraviolet pathogen reduction technologies are also a potential alternative to isotopic blood irradiation. In 2014, the FDA approved two UV systems to treat plasma and platelets, respectively, for pathogen and bacterial reduction.⁴⁴ The approved systems use the UVA wavelength range of illumination (315-400 nm)

³⁹ Bakken, Erik, Katie Cary, Allison Derrick, Ellen Hildebrand, Kyle Schroekenthaler, and Malika Taalbi, “Cost-Benefit Analysis of Switching from Cesium-Chloride to X-ray Blood Irradiators,” (University of Wisconsin-Madison, 2013).

⁴⁰ Kopolovic, I., et al., “A systematic review of transfusion-associated graft-versus-host disease,” *Blood*, 2015, 126(3):406-414.

⁴¹ Whitaker, Barbee, Srijana Rajbhandary, Andrea Harris, *The 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey Report*, AABB, December 18, 2015, page 63, Available at <https://www.aabb.org/research/hemovigilance/bloodsurvey/Documents/2013-AABB-Blood-Survey-Report.pdf>.

⁴² Bakken, Erik, Katie Cary, Allison Derrick, Ellen Hildebrand, Kyle Schroekenthaler, and Malika Taalbi, “Cost-Benefit Analysis of Switching from Cesium-Chloride to X-ray Blood Irradiators,” (University of Wisconsin-Madison, 2013).

⁴³ Radiological Devices Advisory Panel, Blood Irradiators – Unclassified: Executive Summary, accessed August 28, 2015.

⁴⁴ One manufacturer, Cerus Corporation, has two separate systems, the INTERCEPT Platelet system and the INTERCEPT Plasma system, which are used separately to treat platelets and plasma, respectively. Both systems have received FDA approval in December 2014. Other manufacturers are expected in the U.S. market in the future. The approved UV systems are labeled to potentially reduce the risk of TA-GvHD. They are defined in the AABB standards to replace gamma and x-ray radiation for prevention of TA-GVHD and have done so for platelets in some U.S. blood centers.

with the molecule amotosalen, which interacts with nucleic acid to form irreversible adducts that inhibit pathogen and cellular replication. The approved UV systems are labeled to indicate that they potentially reduce the risk of TA-GvHD. In 2016, the AABB modified its United States standards⁴⁵ to indicate that the use of approved pathogen reduction systems meets the standard for prevention of TA-GvHD. A red cell system needs FDA approval in the United States before cesium-137 systems can be completely replaced.⁴⁶ Table 1.1 provides an overview of the approved applications and treatments achieved by each type of irradiation device.

Table 1.1: Comparison of Systems for Blood Irradiation and Pathogen Reduction by Application and Outcome

Key	Isotopic Technology	Non-Isotopic Alternative Technologies		
	Gamma (Cs-137) Irradiator	X-ray Irradiator	UV Pathogen Reduction ⁴⁷ Amotosalen	UV Pathogen Reduction Riboflavin
● CE Marking & FDA approved for use				
⊘ CE Marking only, in clinical development for FDA				
Whole Blood	●	●		⊘
Platelets	●	●	●	⊘
Plasma	●	●	●	⊘
Red Blood Cells	●	●		
Transfusion-Associated Graft-versus-Host Disease ⁴⁸		●	●	⊘
Transfusion-Transmitted Infections ⁴⁹			●	⊘
Transfusion-Associated Adverse Reactions ⁵⁰			●	⊘

⁴⁵ Regan, Donna and Miriam A. Markowitz, American Association of Blood Banks, "Changes to the 30th edition of *Standards for Blood Banks and Transfusion Services*," Association Bulletin #16-05 to AABB Members, March 17, 2016.

⁴⁶ Radiological Devices Advisory Panel, Blood Irradiators – Unclassified: Executive Summary, accessed August 28, 2015.

⁴⁷ One manufacturer, Cerus Corporation, has two separate systems, the INTERCEPT Platelet system and the INTERCEPT Plasma system, which are used separately to treat platelets and plasma, respectively. Both systems have received FDA approval in December 2014. Other manufacturers are expected in the U.S. market in the future. The approved UV systems are labeled to potentially reduce the risk of TA-GvHD. They are defined in the AABB standards to replace gamma and x-ray radiation for prevention of TA-GVHD and have done so for platelets in some U.S. blood centers.

⁴⁸ CE Marking incorporates recognition that these technologies may be used for the prevention of TA-GVHD.

⁴⁹ 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 (i.e., *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*).

⁵⁰ Transfusion-associated adverse reactions include allergic transfusion reactions, febrile transfusion reactions, and immunization to human leukocyte antigens (HLA).

Self-Shielded Gamma Irradiators

Self-shielded irradiators expose blood products to high doses of gamma radiation. There are over 400 commercial isotope-containing blood irradiators in the United States—most use CsCl sources, while about 5 percent use high-activity cobalt-60.⁵¹

To irradiate blood, a technician places the blood container—usually bags—in a canister, then loads the canister into the device. Once the target blood products are in place, an electronic elevator and shutter system automatically shields the operator as it moves the canister into a line-of-sight position with the radioactive material. The device rotates the canister to ensure a uniform exposure to the high-energy gamma radiation emitted by the material. The blood must be exposed to a dose of 25 Gy or greater to the midpoint of the target to meet FDA requirements.⁵²

Cesium-137 blood irradiators are typically heavy devices, due to the lead shielding required to safely house the high-activity CsCl sources. Eight models are approved for use in the United States. Most new commercial devices weigh approximately 3,000 pounds and use multiple sources totaling 3,000 Ci of encapsulated CsCl, while larger models weigh more than 4,000 pounds and house CsCl sources exceeding 5,000 Ci at purchase. Cobalt-60 devices weigh approximately twice as much as most cesium-137 blood irradiators, often exceeding 5,000 pounds, due to the shielding required for the particularly high-energy isotope.

X-ray Irradiators

The FDA has found x-ray devices from three manufacturers to be “substantially equivalent” to gamma source irradiators in preventing TA-GvHD, awarding them a 510(k) clearance. The FDA can grant equivalence to premarket medical devices that meet several conditions, including a demonstration that a device with different technological characteristics does not “raise new questions of safety and effectiveness” and is “at least as safe and effective as the legally [U.S.] marketed device.”⁵³ If all conditions are met, the device will receive a 510(k) clearance or premarket notification.

All three equivalent x-ray devices are commercially available in the United States. For a full table of the FDA’s findings on equivalence for gamma and x-ray irradiation devices and their indications for use, see [Appendix 1](#).

X-ray irradiator use in the United States is expanding; however, beyond the rate of participation in the DOE/NNSA CIRP there is limited national tracking of adoption rates or market distribution, which is considered proprietary information by manufacturers. Although device configurations vary, x-ray irradiators typically use a conventional x-ray tube system of two tubes enclosed in a lead-shielded container. To ensure a uniform radiation dose without target rotation, the device may use two x-ray tubes, one on each side of the chamber in which the target container is placed. In one newer design, carousels rotate to uniformly expose target blood to ionizing radiation generated by an x-ray tube in a 360-degree output around a cylindrical design. In general, electronic systems power the x-ray tubes and operate timers to control interlocks and

⁵¹ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008), page 35.

⁵² Ionizing radiation includes not only the gamma radiation produced by radioactive materials, but also the energy produced by x-rays, as well as the higher ultraviolet part of the electromagnetic spectrum. The amount of energy absorbed by matter exposed to ionizing radiation is generally expressed in units of ‘gray’ (Gy). One centigray (cGy) is equal to one one-hundredth of a single Gy. Exposure of 2500 cGy to the midpoint of a target ensures that no part of the target receives less than the minimum 1500 cGy required for potentially harmful lymphocyte elimination.

⁵³ “Premarket Notification 510(k),” U.S. Food and Drug Administration, last updated September, 16, 2015, <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/>.

exposure. X-ray devices typically weigh approximately 2,000 pounds, with dimensions similar to cesium-137 gamma irradiators.

Continued industry R&D is underway to improve the performance of x-ray irradiators and to develop flat-panel x-ray sources, which are expected to come to market in 2019 and 2020.

Ultraviolet Pathogen Reduction

Ultraviolet (UV) pathogen reduction technology was introduced to the United States market in 2014 but has been in use in many countries since the early 2000s. Whole blood, plasma, platelet, and red blood cell components treatment to inactivate pathogens has received the CE Marking,⁵⁴ the legal requirement to place a medical device on the market in the European Union (EU).⁵⁵ One UV system, Mirasol, received the CE Marking for TA-GvHD prevention for whole blood in September 2015. The amotosalen-Ultraviolet A (UVA) systems for platelets and plasma (Cerus INTERCEPT) received the CE Marking and specific registration blood component label claims for prevention of TA-GvHD in France, Germany, Switzerland, and Austria.⁵⁶ This system is now in routine use in Sweden.⁵⁷

In 2014, the FDA approved two UVA systems—the INTERCEPT Platelet system and the INTERCEPT Plasma system from the Cerus Corporation—to treat plasma and platelets for pathogen reduction. These systems are now in use in many blood centers across the United States. They use the molecule amotosalen, which interacts with nucleic acid upon UVA illumination to inhibit pathogen and cellular replication.⁵⁸ Additional systems are expected to become commercially available in the United States within the next 5 years. However, pathogen reduction systems are not yet FDA-approved for treating red blood cells; such approval is necessary before the systems could affect cesium-137 replacement.⁵⁹ The UVA-amotosalen system is recognized in the 2016 AABB United States standards for the prevention of TA-GvHD equal to gamma-source irradiation.⁶⁰

UV systems could potentially provide cost savings in relation to other blood irradiation systems because they have the added capability to treat blood products for inactivation of bacterial and other pathogen contaminants. In contrast, platelet components treated by gamma or x-ray irradiation for TA-GvHD risk must first undergo an additional process to identify pathogen and bacterial contamination, which adds additional time and cost. A recent study used data from several large hospitals and blood centers to assess potential cost savings related to the use of certain UV systems for pathogen inactivation, primarily resulting from the elimination of the additional testing sometimes necessary for blood products irradiated using gamma

⁵⁴ The CE Marking (an acronym for the French “Conformité Européenne”) certifies that a product has met European Union health, safety, and environmental requirements, which ensure consumer safety. The term initially used was “EC Mark”; it was officially replaced by “CE Marking” in the Directive 93/68/EEC in 1993.

⁵⁵ Some countries require a Class III CE Marking for the use of treated blood products that use pathogen reduction devices.

⁵⁶ Ultraviolet radiation is divided into numerous sub-categories, including Ultraviolet A, B, and C, depending on the energy wavelength. The Ultraviolet A (UVA) spectrum is defined as UV radiation with a wavelength range between 315 and 400 nanometers. Ultraviolet B (UVB) spectrum is defined as UV radiation with a wavelength range between 280 and 315 nanometers. Ultraviolet C (UVC) spectrum is defined as UV radiation with a wavelength range between 100 and 280 nanometers. See International Organization for Standardization, ISO 21348:2007, “Space environment (natural and artificial) – Process for determining solar irradiances,” <https://www.iso.org/standard/39911.html>.

⁵⁷ Sandgren, P. and B. Diedrich, “Pathogen inactivation of double-dose buffy-coat platelet concentrates photochemically treated with amotosalen and UVA light: preservation of in vitro function,” 2015, *Vox Sang* 108(4): 340-349.

⁵⁸ This system has been licensed in Europe and is mandated in Switzerland. In European Union countries that require registration of blood products treated with pathogen reduction devices (France, Germany, Switzerland, and Austria), there are specific label claims for replacement of gamma irradiation to prevent TA-GvHD.

⁵⁹ One red cell system (Cerus Corporation) is in clinical development in the United States (Phase 2 completed). This system does not utilize UV light for pathogen and leukocyte inactivation.

⁶⁰ Regan, Donna and Miriam A. Markowitz, American Association of Blood Banks, “Changes to the 30th edition of *Standards for Blood Banks and Transfusion Services*,” Association Bulletin #16-05 to AABB Members, March 17, 2016.

sources. The assessment also identified the potential for additional savings should the FDA approve seven-day platelet storage, which may be enabled by pathogen inactivation systems.⁶¹ While the study concluded that the per-unit savings from system implementation could be significant, the authors noted that the savings, if any, would vary depending on the operational specifics at these facilities.⁶²

The UVA pathogen reduction system has a much smaller footprint than that of gamma and x-ray irradiators, with dimensions similar to those of a desktop scanner, and it is transportable. To start the pathogen reduction process with amotosalen-UVA systems, donor blood products are treated with a synthetic photochemical (amotosalen) that, upon UV light exposure, prevents ribonucleic acid-deoxyribonucleic acid (RNA-DNA) replication and inactivates lymphocytes and pathogens. The pathogen reduction process in riboflavin (vitamin B2) UV systems—used in the EU but not yet licensed in the United States—uses UVA, ultraviolet B (UVB), and ultraviolet C (UVC) illumination and disrupts RNA-DNA through the formation of reactive oxygen species.

Technology Purchase and Replacement Considerations

X-ray irradiators deliver ionizing radiation of 25 Gy or greater to the midpoint of the target product, meeting the same medical requirements as gamma irradiators for TA-GvHD prevention. The amotosalen-UVA system for plasma and platelets is recognized in the AABB standards for the prevention of TA-GvHD as equal to nuclear source irradiation.⁶³ However, a red blood cell system still needs FDA approval in the United States before radioisotope-source devices could be replaced. In this instance, technical requirements would be met, so potential buyers would likely base their purchase/replacement decisions on factors such as their operational workload needs as well as the cost and security factors of each technology. Some users believe that UVA may ultimately be the most reliable and cost-effective alternative.

Cost factors are complex and exist at different stages of each technology's lifecycle. Current, limited cost-benefit analyses have only compared x-ray and cesium-137 irradiators; as such, the discussion here focuses on these two technologies. Additional analysis of both x-ray and UV pathogen reduction system costs is an avenue for further research.

Lifecycle Technology Costs

Cesium-137 devices have been in use since the 1960s and have a long operational history, having been known to last for more than 30 years.⁶⁴ While there is a lack of formal lifespan data for x-ray irradiators, informal estimates put the lifespan for x-ray irradiators at approximately 10 to 15 years.⁶⁵ This means a facility may have to purchase multiple replacement x-ray components and devices to equate to the lifespan of one cesium-137 irradiator. However, the speed with which cesium-137 irradiators can treat blood products does slow with age as isotopes decay, affecting a machine's capacity over time.

⁶¹ U.S. Department of Health and Human Services (HHS), "Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion: Draft Guidance for Industry," March 2016, <http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM425952.pdf>.

⁶² McCullough, J., Goldfinger, D., Gorlin, J., Riley, W. J., Sandhu, H., Stowell, C., Ward, D., Clay, M., Pulkrabek, S., Chrebtow, V. and Stassinopoulos, A., "Cost implications of implementation of pathogen-inactivated platelets," *Transfusion*, 2015, 55: 2312–2320. doi:10.1111/trf.13149.

⁶³ Regan, Donna and Miriam A. Markowitz, American Association of Blood Banks, "Changes to the 30th edition of *Standards for Blood Banks and Transfusion Services*," Association Bulletin #16-05 to AABB Members, March 17, 2016.

⁶⁴ Leitman, Susan F., "Role of Cesium-137 Chloride Irradiators in Transfusion Medicine," Nuclear Alternate Technology Working Group (Washington, DC: April 7, 2015).

⁶⁵ U.S. Nuclear Regulatory Commission, Cost-Benefit Analysis for Potential Alternative Technologies for Category 1 and 2 Radioactive Sources, by ICF Incorporated, L.L.C., (Rockville, MD: 2009), page 36.

The initial purchase costs between x-ray and cesium-137 irradiators are similar, but the lifecycle costs for the two systems differ. Inflation, variable costs, and sunk costs must also be considered for each device. An overview of cost and operations considerations is included below. [Appendix 2](#) contains a list of associated costs to consider, including indirect costs such as utilities and labor, from a cost-benefit analysis of x-ray and gamma irradiators.

Purchase

The purchase prices of large cesium-137 and x-ray irradiators are similar; they typically cost between \$200,000 and \$350,000. The devices have similar weight-related infrastructure requirements, such as reinforced flooring to support heavy lead shielding. However, cesium-137 devices may require the installation of additional safety and security controls, such as access control systems and barriers. Individual states and cities may also have additional security requirements for the transportation of cesium-137 devices (e.g., police escorts) that must be paid for by the licensee. CIRP offers cost-share support for the voluntary replacement of gamma irradiators with x-ray devices (typically 50 percent of the replacement device cost).

DOE/NNSA Cesium Irradiator Replacement Program (CIRP)

Efforts to replace Category 1 and 2 radioactive sources with effective alternatives have become increasingly successful for blood irradiation, in large part due to technological advances that have improved the reliability and cost of x-ray irradiation devices. Furthermore, DOE/NNSA offers cost-share support for Cs-137 device replacement (typically 50 percent of the new device cost) through its CIRP. CIRP is entirely voluntary. Program participants are responsible for selecting the non-isotopic replacement device that meets their technical, operational, and financial requirements; costs related to new device training, as well as the purchase of a warranty or maintenance agreement for the new device, if applicable, are the responsibility of the CIRP participant organization. CIRP support includes removal and disposal of the CsCl irradiator by the NNSA Off-Site Source Recovery Program. To help ensure that program participation supports permanent risk reduction, CIRP participants sign a disposition agreement acknowledging the purpose and goal of the project. In addition, disbursement of financial incentives to CIRP participants takes place only after the removal of the CsCl device is complete.

The success of CIRP was evidenced in December 2017, when licensees from all medical and academic facilities in New York City (part of the New York Agreement State program) committed to transitioning from Cs-137 blood irradiators to x-ray devices through CIRP. In addition, the University of California has committed to replacing the cesium blood irradiators at all its medical facilities with x-ray devices. In 2019, Vitalant, a major U.S blood supplier, committed to replacing 100 percent of its blood irradiators with x-ray devices in the next few years. As of June 2019, the CIRP program has replaced, or is in the process of replacing, approximately 35 percent and 25 percent respectively of the CsCl and Co-60 blood and research irradiators that were in use when the program began in 2015.

Congress directed DOE/NNSA in the fiscal year (FY) 19 National Defense Authorization Act (NDAA) by providing budgetary planning direction with the goal of “eliminating the use of blood irradiation devices in the United States that rely on cesium chloride by December 31, 2027 under the current CIRP program structure.” However, the goal per the FY19 NDAA “is voluntary for owners of blood irradiation devices.”¹

¹ H. R. 5515, “John S. McCain National Defense Authorization Act for Fiscal Year 2019,” Subtitle D, SEC. 3141. “Acceleration of Replacement of Cesium Blood Irradiation Sources,” August 13, 2018, <https://www.congress.gov/bill/115th-congress/house-bill/5515>.

Installation and Operation

The installation of alternative technologies may require infrastructure refurbishment or construction—particularly for sites that are replacing existing gamma irradiators—but the requirements will be highly site specific. X-ray irradiators have similar footprints to cesium-137 devices. They may require additional infrastructure redesign (e.g., adding access to water lines and chillers for cooling, electrical capacity, and air conditioning) depending on the room design and the make of the purchased device. Some newer models have internal cooling and may not require infrastructure redesign. Facilities may also need to buy more than one x-ray machine based on their needs; this is expanded upon in the next subsection.

The UV pathogen reduction system has a much smaller footprint—similar to a desktop scanner—but may require other reorganization of storage and processing areas. Additional analysis of infrastructure requirements for UV pathogen reduction is required.

Maintenance and Operational Reliability

X-ray irradiators introduce new maintenance and reliability concerns, including the life of the two x-ray irradiator tubes, the water-cooling system (whether self-contained or via external line), preventative maintenance needs, quality assurance, program implementation, and the lifespan of the device.

For x-ray devices, manufacturer service contracts often cover parts replacement, preventative maintenance, and dosimetry/calibration. Service contract cost depends on the volume and usage of the x-ray device, and may range from \$6,000 to \$20,000 per year or more, according to some reports.⁶⁶ High-throughput facilities may require more frequent parts replacement or maintenance than the contract allows, or facilities may need to install multiple devices to ensure there is no downtime. Cesium-137 irradiators will also carry service contract costs, but they are typically less expensive—from \$1,000 to \$14,000 per year—because the devices need fewer replacement parts.⁶⁷

Continued commercial and R&D efforts are focusing on new devices and system components to help alleviate some of the operational reliability concerns. A 2013 American Association of Physicists in Medicine (AAPM) survey of member institutions that use cesium-137 or x-ray blood irradiators found concerns over reliability and sustainability were the primary barrier to purchase and/or conversion.⁶⁸ A 2013 workshop report by the World Institute of Nuclear Security (WINS) also identified perceived or actual reliability issues, required changes to operations, costs, and complacency of standard practice as major barriers to transitioning to alternative technologies.⁶⁹ Potential downtime due to power interruption is a concern for x-ray devices; cesium-137 devices do not rely on an external power source to remain operational.⁷⁰

⁶⁶ Bakken, Erik, Katie Cary, Allison Derrick, Ellen Hildebrand, Kyle Schroeckenthaler, and Malika Taalbi, “Cost-Benefit Analysis of Switching from Cesium-Chloride to X-ray Blood Irradiators,” (University of Wisconsin-Madison: 2013).

⁶⁷ Ibid.

⁶⁸ American Association of Physicists in Medicine (AAPM), “2013-10-17 AAPM Irradiator Survey—Final,” presentation to the Nuclear Alternate Technology Working Group, April 7, 2015; While the survey had a limited sample size, it illustrates the main concerns and considerations for alternative technologies.

⁶⁹ World Institute of Nuclear Security, “Alternative Technologies to Radioactive Sources,” Workshop Report, Brussels, October 8-9, 2013; American Association of Physicists in Medicine (AAPM), “2013-10-17 AAPM Irradiator Survey—Final,” presentation to the Nuclear Alternate Technology Working Group, April 7, 2015.

⁷⁰ Some Cs-137 irradiators may have components that require electricity for operation, such as the rotator, elevator and timer.

Device Ability to Meet Site and Application Requirements

In comparison with cesium-137 blood irradiators, x-ray irradiators have been reported to have increased maintenance requirements and potential downtime across their lifetime.⁷¹ These reports did not include information on whether a site has a high blood unit throughput, the age or average workload for the device in question, or the make and model of the x-ray irradiator. In many cases sites may be heavily operating the x-ray irradiator, with a correspondingly higher probability of device failure. In addition to analyzing cost considerations, sites must complete a product throughput capacity assessment to ensure devices will meet their needs and maintain necessary operations. Due to differences in dose rates and/or volume capacity, an x-ray device may operate at a different product throughput capacity than a similar cesium-137 device.

It is important to consider the product throughput capacity needs of each specific site when determining whether an x-ray irradiator is appropriate for a facility. This may include an estimate of average blood unit throughput, forecasted blood unit needs, new device capacity, and/or expected operational lifetime. There is a DOE-developed tool for facilities to compare the number of cesium-137 and x-ray irradiators needed to accommodate their individual operations.⁷²

The use of UV pathogen reduction systems may include potential cost offsets due to their ability to replace bacterial detection testing; cytomegalovirus (CMV) serology tests; and testing for newly emerging pathogens, such as Zika and dengue.⁷³ However, more data are needed.

Administrative and Regulatory Costs

Cesium-137 irradiators come with greater regulatory and licensing requirements than x-ray devices. In March 2013, the NRC published a final rule in the Federal Register to increase security requirements for the use and transport of risk-significant quantities of radioactive material, including the types of cesium-137 and cobalt-60 sources used for blood irradiation.⁷⁴ The rule contains requirements for background investigations; access controls; security plans; immediate detection, assessment and response to unauthorized access; tracking of shipments; security barriers; and other requirements. All licensees who possess subject radioactive material are under the current regulatory oversight of the NRC or applicable Agreement State.

Many facilities—especially hospitals—maintain institutional security for the protection of staff, patients, and information. However, similar to protection requirements for biological materials and controlled substances, the protection of radioactive materials requires additional security and costs. The NRC initially estimated that the average cost of implementation for licensees would be approximately \$21,736 annually to fully implement the rule.⁷⁵ However, licensees have reported varying cost estimates, both lower and higher. These costs depend on the number of individuals who are granted unescorted access to the device, the number of procedures that must be newly developed, the actual security measures that are used to meet the requirements, and the extent of training. Licensees have already been subject to these requirements for

⁷¹ Leitman, Susan F, “Role of Cesium-137 Chloride Irradiators in Transfusion Medicine,” Nuclear Alternate Technology Working Group (Washington, DC: April 7, 2015).

⁷² This tool can be accessed at <https://orsbloodtool.sandia.gov/Calculator/index.html>.

⁷³ U.S. Food and Drug Administration (FDA), Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion Transmission of Zika Virus, February 2016, accessed June 29, 2016, available at <https://www.govinfo.gov/content/pkg/FR-2016-02-19/pdf/2016-03393.pdf>.

⁷⁴ 10 C.F.R. Part 37, “Physical Protection of Byproduct Material” [NRC 2013f].

⁷⁵ U.S. Nuclear Regulatory Commission, “Regulatory Analysis for Final Rule: Physical Protection of Byproduct Material, (10 C.F.R. Parts 20, 30, 32, 33, 34, 35, 36, 37, 39, 51, 71, and 73),” (Washington, DC: December 2011), available at <http://www.nrc.gov/reading-rm/doc-collections/commission/secys/2011/2011-0170scv.pdf>.

more than a decade, so may have compliant procedures and training already in place. The actual costs also depend on the number of sealed sources possessed by a licensee and the location of the sources relative to other sources and assets at the facility.

Additional costs include an annual program review and the maintenance and testing of security-related equipment. The review is important for licensees to evaluate the effectiveness of the program and to ensure that requirements are being implemented. Maintenance and testing also ensure equipment is operational and available when needed.⁷⁶

While sites may still be required to pay for the registration of x-ray devices in a state-based regulatory system and x-rays require an annual state-regulated safety evaluation, neither x-ray irradiators nor UV pathogen reduction systems require the same security regulations as cesium-137 irradiators; this reduces the regulatory, financial, and administrative burden on site personnel. Additionally, little training would be required to convert cesium-137 irradiators to x-ray irradiators, outside of rewriting point-of-care or laboratory procedures for operators. In contrast, due to differences in how the technology operates and its recent introduction to the United States market, UV pathogen reduction technology may require new equipment training and competency assessment for operators. However, it eliminates the use of ionizing radiation all together when the technology for red blood cells and whole blood is available.

The 2013 AAPM survey of cesium-137 or x-ray blood irradiator users found that relief from regulatory compliance and financial burdens most strongly influences a facility's decision to purchase or convert to x-ray irradiators.⁷⁷ The 2013 WINS report identified regulatory bans as one of the primary international reasons for conversion.⁷⁸

Disposal Costs and Considerations for Sealed Source Irradiators

The proper disposal of radioactive materials used by the private sector is the responsibility of the licensees who benefit from them commercially. However, commercial disposal access challenges and security concerns related to high-activity sources has led to a temporary increase in government involvement, including the assumption of significant costs related to disposal.

Source Disposal

As indicated in federal legislation, the proper disposal of radioactive materials used by the private sector is the responsibility of the licensees who benefit from them commercially.⁷⁹ However, due to commercial disposal access challenges and security concerns, the Federal Government has recovered and disposed of tens of thousands of disused and unwanted Category 1 and 2 sources across the past 20 years at no cost to

⁷⁶ U.S. Nuclear Regulatory Commission, "Regulatory Analysis for Final Rule: Physical Protection of Byproduct Material, (10 C.F.R. §§ 20, 30, 32, 33, 34, 35, 36, 37, 39, 51, 71, and 73)," (Washington, DC: December 2011).

⁷⁷ American Association of Physicists in Medicine (AAPM), "2013-10-17 AAPM Irradiator Survey—Final," presentation to the Nuclear Alternate Technology Working Group, April 7, 2015; While the survey had a limited sample size, it illustrates the main concerns and considerations for alternative technologies.

⁷⁸ World Institute of Nuclear Security, "Alternative Technologies to Radioactive Sources," Workshop Report, Brussels, October 8-9, 2013; American Association of Physicists in Medicine (AAPM), "2013-10-17 AAPM Irradiator Survey—Final," presentation to the Nuclear Alternate Technology Working Group, April 7, 2015.

⁷⁹ Commercially generated radioactive waste in the United States (with the exception of spent fuel used in commercial power generation) is classified according to NRC regulations as Class A, B, C, or "greater-than-Class C" (GTCC) low-level radioactive waste (LLRW), depending on its radioactivity concentration and half-life. The Low-Level Radioactive Waste Policy Amendments Act of 1985 (LLRWPA) makes States responsible for providing disposal options for Class A, B, and C LLRW generated within their borders, while DOE is responsible for providing disposal options for Greater-than-Class C (GTCC) LLRW, including the implementation of mechanisms to ensure that the commercial entities who benefit financially from the activities resulting in GTCC waste generation will bear reasonable costs for its disposal.

users.⁸⁰ This has included cesium-137 and cobalt-60 gamma irradiation devices, which remain highly radioactive even after the source material has decayed to the point that the device is no longer effective.

Recently updated NRC disposal guidance enables radioactive material licensees to dispose of many Category 2 cesium-137 sources at currently operational commercial radioactive waste disposal facilities.⁸¹ This likely includes cesium-137 irradiator sources up to the ~957 Ci Class C limit for the material. The guidance also enables commercial disposal of most or all Category 1 and 2 cobalt-60 sources as Class A or B waste due to their short half-life. In addition, DOE has made significant progress toward establishing a disposal pathway for Greater-than-Class C (GTCC) waste, including the highest activity cesium-137 sources used in blood and research irradiators.

As commercial disposal options for Category 1 and 2 sources become increasingly available, access to subsidized disposal may be limited. As a result, significant gamma irradiator lifecycle costs will shift back to commercial users. Although the ultimate cost structure that will apply to GTCC sources remains uncertain, disposal fees for Class A, B, and C waste at currently operational commercial disposal facilities are based primarily on the volume and Ci of the waste.

⁸⁰ Pending the availability of commercial disposal options, the National Nuclear Security Administration (NNSA)/Off-Site Source Recovery Project (OSRP) recovers and disposes of high-activity sources in the interest of National security, public health, and safety at Federal facilities primarily intended for the disposal of waste generated by the U.S. government. These sites operate under different legislative authorities than commercial disposal facilities and are prohibited from accepting waste, including sealed sources, directly from commercial radioactive waste generators. Commercial radioactive material licensees may register their sources with NNSA/OSRP, which prioritizes them for recovery according to criteria determined in consultation with the NRC.

⁸¹ U.S. Nuclear Regulatory Commission. "Concentration Averaging and Encapsulation Branch Technical Position, Revision 1," Volumes 1 and 2. February 2015. (ADAMS Accession No. ML12254B065).

Chapter 2: Alternative Technologies for Research Irradiation

Introduction

Irradiation techniques are often used in scientific and medical research; for instance, in support of in vitro and in vivo—inside or outside of animal specimens—biomedical research to further the understanding of biological research science. This research typically exposes cellular materials to radiation to evaluate different scientific hypotheses. There are three primary applications for this radiobiological research:

- **Cell culture studies:** Research on deoxyribonucleic acid (DNA) damage and repair, genomic instability, mutagenesis, neoplastic transformation, epigenetic changes, co-culture responses, immune response, non-cancer effects, and non-targeted effects.
- **Small and large animal studies:** Research on carcinogenesis, tissue reactions (deterministic effects), acute lethality (hematopoietic, gastrointestinal, and central nervous system syndromes), hematological effects, respiratory dysfunction, skin damage, fibrosis, cataracts, radiation-therapy related (low and high dose), genetic susceptibility, normal tissue response, combined injury, immune response, non-cancer effects, and other non-targeted effects.
- **Basic material science and engineering:** Aging studies may also use irradiation. Specific materials or specimens may be exposed to different types and amounts of radiation to better understand the long-term effects of radiation on the material. The exposure of electronics or satellite components to radiation is a primary example. These tests are often conducted with nuclear reactors (for neutrons and gamma exposure) or particle accelerators (for higher energy gamma, proton, and heavy ion exposure), or in very large cobalt-60 cells (for gamma exposure). However, the number of the facilities and devices for these applications is relatively small, and alternatives to nuclear fission reactors are outside the scope of this report.⁸²

Three sources typically generate the ionizing radiation used in bio-medical research irradiation applications: cesium-137 sources produce gamma radiation at 0.662 MeV; cobalt-60 sources produce gamma radiation averaging 1.25 MeV; and x-ray devices that typically generate energy in the range of 50-400 kVp.⁸³ In some cases, researchers may use an e-beam for research irradiation; however these devices are generally much higher-energy and much more expensive than the x-ray and self-shielded gamma irradiators typically used for medical and biological research applications. As a result, x-ray devices are the primary potential replacement technology for cesium-137 and cobalt-60 biological and materials research irradiation sources.

⁸² As a result, the medical and biological research applications described above are the focus of this chapter.

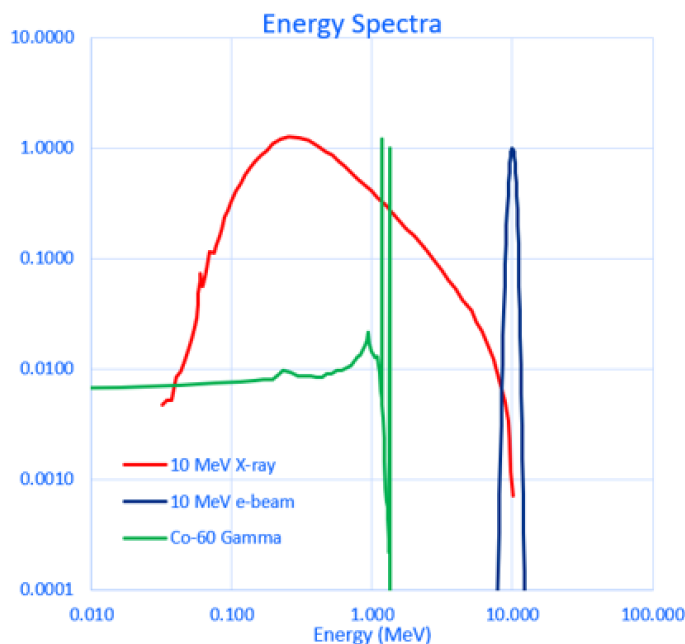
⁸³ The unit kVp refers to “kilovoltage peak.” It describes both the accelerating voltage of the accelerator and the resulting energy of accelerated electrons. kVp is the maximum voltage in an X-Ray tube; keV is the energy of the particle (electron) or wave (x-ray or gamma ray) emitted. The maximum keV of an x-ray or electron from an x-ray tube is numerically equivalent to the kVp of the machine generating it.

Commercially Available Research Irradiation Technologies—Isotopic and Alternatives

Research irradiators—both radioisotopic sources and the most common non-radioisotopic replacements—are technologically very similar to the blood irradiators addressed in Chapter 1. The radioisotopic devices typically use one or more CsCl or cobalt-60 source to expose the target to high doses of gamma radiation. However, relative to blood irradiators, these devices may accommodate a larger range of target shapes and sizes and enable more precise variation in the distance between the source and the target during exposure. In addition, they often use higher activity sources. Individual CsCl research irradiators range from under 1,000 Ci to approximately 20,000 Ci in the largest devices, with most containing 1,200 to 3,000 Ci. Cobalt-60 models are higher-activity devices on average, with some exceeding 30,000 Ci. Approximately 300 gamma research irradiators are in operation in the United States.

As depicted in Figure 2.1 below, the energy distributions for radioisotope, x-ray, and e-beam sources are fundamentally different. Radioisotopes commonly produce peaked spectra, with primary gamma rays at just one or a few energies. For example, the primary gamma rays of cobalt-60 are at 1.173 and 1.333 MeV, and that of cesium-137 is at 0.662 MeV. In contrast, x-rays produce a spectrum that includes x-rays of all energies below the maximum energy and an average energy of about one-third the maximum energy.

Figure 2.1 Comparison of gamma, x-ray, and e-beam energy spectra



Studies using irradiators will have different design requirements depending on their purpose. The requirements typically involve four factors, especially when using live animal targets: PDD, dose rate, size

and type of animal specimen, and energy delivery.⁸⁴ PDD is a measure of how the dose varies with depth within a sample, along an axis in line with the radiation source. In general, higher-energy radiation more effectively penetrates targets, but the PDD will vary depending on the type and extent of the bone, tissue, or other matter it must penetrate, regardless of the radiation source type used. To accurately assess the outcome of a study, researchers must control all four factors within their acceptable margin of error. As a result, these factors are the primary considerations for researchers deciding what type of device to use for an experiment. Additional factors such as researchers' prior training on devices—including dosimetry and research design—and device availability may also affect technology choices.

Because of these factors, the suitability of irradiators for research is highly dependent on the specific needs of the intended research. From a strictly technical standpoint, replacement of gamma research irradiators with current alternatives may be feasible for a significant number of radiobiological research applications, which typically require 1 to 10 Gy/min.⁸⁵ Commercially available x-ray devices can deliver up to 15 Gy/min.⁸⁶ However, because of the differences in PDDs, x-ray technology may not be able to replace radioisotope devices for some research applications.⁸⁷ Additional comparison studies between gamma irradiators and alternative technologies may aid researchers considering a transition from one technology to another.

Self-Shielded Gamma Irradiators

Self-shielded gamma research irradiators are widely used at hospitals, universities, and governmental and commercial facilities that conduct radiobiological or materials research. The devices typically use one or more CsCl or cobalt-60 sources to expose cell cultures, animal specimens, or other targets to high doses of gamma radiation. Approximately 400 gamma research irradiators are in operation in the United States CsCl devices are the more common of the two primary types, with approximately 300 in use. The number of these devices is roughly the same as the number of blood irradiators using CsCl. However, research irradiators use much higher activity sources on average, accounting for two-thirds of the CsCl Ci used in the two applications combined.⁸⁸

Individual CsCl irradiators range from under 1,000 Ci to approximately 20,000 Ci in the largest devices, with most containing 1,200 to 3,000 Ci. Cobalt-60 models are higher activity devices on average, with some exceeding 30,000 Ci.⁸⁹ Typical CsCl devices weigh between 1,500 and 6,000 pounds (lbs), with floor-loading requirements ranging from roughly 100 to 600 lb/sq. ft. Cobalt-60 models may be several times heavier due to the shielding requirements for the high-activity and high-energy devices.

Most cesium-137 and cobalt-60 research irradiators function similarly to blood irradiators that use similar sources. A specimen or material is front-loaded into the device, which then uses an electronic control system to move the target and source into a safe position for the timed exposure. Targets are generally rotated while in this position to provide a more uniform dose. However, relative to blood irradiators, these devices may

⁸⁴ Dose rate is the amount of radiation energy deposited in a target mass in a given amount of time. It is an important metric because it is used to determine the flow rate of materials through an irradiation system, thus affecting things such as productivity, profitability, worker time, patient comfort, etc.

⁸⁵ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008), 96.

⁸⁶ Garrison, Lance, Arden Dougan, and Allen Bakel, "Research and Development to Enable the Replacement of Radioisotope Sources," Proceedings of the Institute for Nuclear Materials Management (2016).

⁸⁷ Ibid.

⁸⁸ Nuclear Regulatory Commission (NRC), "Strategy for the Security and Use of Cesium-137 Chloride Sources," SECY-08-0184, November 24, 2008, page 8.

⁸⁹ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008), 35.

accommodate a larger range of target shapes and sizes. They also enable precise variation in the distance between the source and the target during exposure.

Dose rates are typically 0.5 to 10 Gy/min at defined positions within the irradiation chamber, although the largest devices may deliver several hundred Gy/min. The dose rate depends on the source type and its current Ci content or activity. For any given source, the dose rate will vary depending on the source-to-sample distance, the physical dimensions of the source, and whether the source field is isotropic (extending in all directions) or shaped by a collimating device which narrows a beam of particles or waves. Traditional x-ray irradiator designs are point-source geometry and are collimated in one direction, and typical cesium-137 irradiator designs involve a line-source geometry with an isotropic field.

X-ray Irradiators

As with x-ray blood irradiator use, x-ray research irradiator use in the United States is expanding, however, beyond the rate of participation in the DOE/NNSA CIRP there is limited national tracking of adoption rates or market distribution. There are currently at least five domestic research x-ray manufacturers offering models from 160 kVp to 320 kVp. These devices provide up to approximately 15 Gy/min.

X-ray research irradiators function in generally the same way as x-ray devices used for blood irradiation, using electricity and an x-ray tube to generate electrons aimed at a tungsten or tantalum target. The interaction of the electrons with the target produces x-rays, which irradiate the specimen chamber. The devices typically have a front-loading cabinet configuration with similar or slightly larger dimensions as their gamma counterparts. They enable distance variation from the x-ray source, and a turntable may be used to increase dose uniformity. Some also include an imaging feature to provide x-ray images of specimens to researchers, both for targeting and for visual assessment.

Although similar in size and shape, these devices weigh less on average than their gamma counterparts, with available models weighing from less than 1,000 to more than 4,000 lbs, depending on their energy output. Typically, 230-volt electrical service outlets are used to power the devices, and many have emergency power batteries in case of grid-supply interruption. In the United States, the industrial standard is 208-volt single phase; therefore, if the x-ray model does not convert from 208 to 230 volts internally, then the room's electrical outlet would have to be upgraded to 230 volts. The higher kVp models include cooling systems that typically circulate air, water, and/or oil for heat dissipation. As a result, connection to an external water source and additional room air conditioning are sometimes required.

In addition to these more common x-ray tube models, a new x-ray technology is under development that uses a flat-panel system instead of tubes for x-ray generation. The design enables a highly uniform dose across a broad surface and sustained operation at high-power levels without the maintenance challenges that current x-ray tubes experience under similarly intense conditions. Three flat-panel systems are under development to address different research needs, including a digitally interfacing model that will allow users to vary the intensity, timing, and precise location of x-rays.⁹⁰ The devices are expected to come to market in 2019 with target prices of \$175,000 to \$275,000.⁹¹

⁹⁰ "Company," Stellararray, accessed August 16, 2016, <http://stellar-ray.com/>.

⁹¹ 2017 DOE Small Business Investment Research (SBIR) Program Review.

Linear Accelerators

Linear accelerators (linacs) are not commonly used in small-animal research; they have different capabilities and are much more expensive than self-contained gamma and x-ray irradiators. Therefore, they are not a direct replacement for these technologies.

Technology Purchase and Replacement Considerations

Due to the wide variation in research applications, replacement considerations for research irradiators are different than those for blood irradiators and are typically related to specific research requirements. However, for research areas in which x-rays and gamma rays have been demonstrated as equally effective, lifecycle costs may also influence decisions. While device selection will be specific to each research design, this section outlines general considerations for device selection.

Lifecycle Technology Costs

Purchase

A one-to-one comparison of x-ray and gamma devices is challenging due to variation in research uses, as well as the different capabilities provided by some of the newer irradiator models of both types. A 2015 comparison of x-ray and gamma radiation used in small animal research applications reviewed price quotes for x-ray and cesium-137 devices, indicating the initial purchase price of the x-ray irradiator is about one sixth that of a cesium device.⁹²

However, the price discrepancy in this case may not be typical. For example, a review of National Institutes of Health (NIH) Shared Instrumentation Awards from 2006 to 2015 lists 21 awards for research irradiator purchases—seven for x-ray irradiators, 11 for cesium-137 devices, and three unspecified devices.⁹³ The cost of these devices ranges from \$111,075 to \$600,000 for an x-ray irradiator for small-animal research applications or cell irradiation. The gamma irradiators listed range from \$233,915 to \$500,000 but are not tied to specific applications. CIRP offers cost-share support for the voluntary replacement of self-contained gamma blood and research irradiators with x-ray devices.

Installation and Operation

The primary installation costs for gamma irradiators are related to the logistical challenges of safely and securely moving the very large and heavy radiological devices in a hospital or university campus setting. However, these costs are typically low relative to the purchase price of the device, which includes costs related to device transportation from the manufacturer.

X-ray irradiators use electricity to produce radiation; as a result, installation of these devices produces different logistical challenges than those related to gamma devices. The necessary electricity and water-

⁹² Gibson, Brian W. et al., "Comparison of Cesium-137 and X-ray Irradiators by Using Bone Marrow Transplant Reconstitution in C57BL/6J Mice," *Comparative Medicine*, Vol. 65, No. 3, June 2015, pages 165–172: "After reviewing quotes, we estimate that the initial purchase price of an X-ray irradiator is about one sixth that of a cesium source. These figures do not include the costs of shipping, installation, or disposal of old active-source machines, and thus actual start up costs are much higher. Annual maintenance as well as annual or semiannual dosimetry assessment costs are relatively comparable between the 2 sources."

⁹³ National Institutes of Health, Office of Infrastructure Research, "Shared Instrumentation Awards," accessed August 26, 2016, https://dpcpsi.nih.gov/orip/diic/fy_sig_awards.

cooling requirements for the devices may require costly infrastructure modifications. Once installed, there are variable costs for use of these devices depending on user demand; for example, relative to blood irradiators, these devices are less likely to be in constant use. Research programs vary regarding the number of device users and the amount of use time required, and research requiring relatively low levels of radiation delivered across longer time periods will require more electricity and maintenance than will experiments with shorter, fixed irradiation cycles. Although the electricity required to operate a gamma irradiator is negligible, cobalt-60 research irradiators require periodic source replacement due to the five-year half-life of the material, adding additional expense.

A related operational consideration is the rate at which an irradiator delivers its dose to the target. Depending on the research needs and the irradiator models compared, cesium-137 irradiators may provide a higher dose rate, allowing a more productive research schedule. As the source decays, however, the dose rate of a gamma irradiator will decrease, whereas the dose rate for an x-ray irradiator remains nearly constant across its operational lifetime.

Maintenance and Operational Reliability

Since medical research irradiators are very similar to blood irradiators, their maintenance and operational reliability are also similar. See the “Maintenance and Operational Reliability” section in Chapter 1 for an overview. One difference between irradiators for these two applications is the frequency of irradiator use. Blood irradiators may see a wide variation in day-to-day operation time, but weekly averages are relatively stable. Research irradiator up-time varies widely from one facility to the next; some have tens of researchers coordinating frequent usage while others have only a single or a few researchers who require infrequent machine use. The relatively higher or lower frequency of use compared with blood irradiators could result in differing maintenance needs, with some components in infrequently used irradiators lasting longer. The 2015 comparison of x-ray and gamma radiation used in small-animal research noted that “[a]nnual maintenance as well as annual or semiannual dosimetry assessment costs are relatively comparable between” gamma and x-ray devices.⁹⁴

Research Requirements

PDD is an important technical specification for research irradiation. It is the relative dose delivered as a function of target depth, normalized to the peak dose at any depth. The PDD for any given application depends on the radiation energy distribution, the composition of the target sample, the beam field size, and the source-to-target distance. The PDD profile is also highly dependent on source geometry; traditional x-ray sources radiate from a single point, whereas many cesium-137 sources are shaped like long pencils or cylinders.

Despite the energy spectrum and geometry differences, cesium-137 and x-ray PDD profiles can be quite similar. For the irradiators commonly used in medical research, less than 400 kVp, the PDD is maximum at or just below the target surface and decreases as depth increases. Sample PDDs for x-ray and gamma radiation (both consisting of photons) can be seen in Figure 2.2. The 100 kVp and 400 kVp PDDs are representative of research irradiators, while the 10 MV and 22 MV PDDs are relevant for other applications, including the cancer treatment and irradiation applications using e-beam technologies discussed in following chapters. The PDD from cesium-137 is not pictured but lies between the cobalt-60 and 400 kVp curves.

⁹⁴ Gibson, Brian W. et al., “Comparison of Cesium-137 and X-ray Irradiators by Using Bone Marrow Transplant Reconstitution in C57BL/6J Mice,” *Comparative Medicine*, Vol 65, No 3, June 2015, pages 165–172.

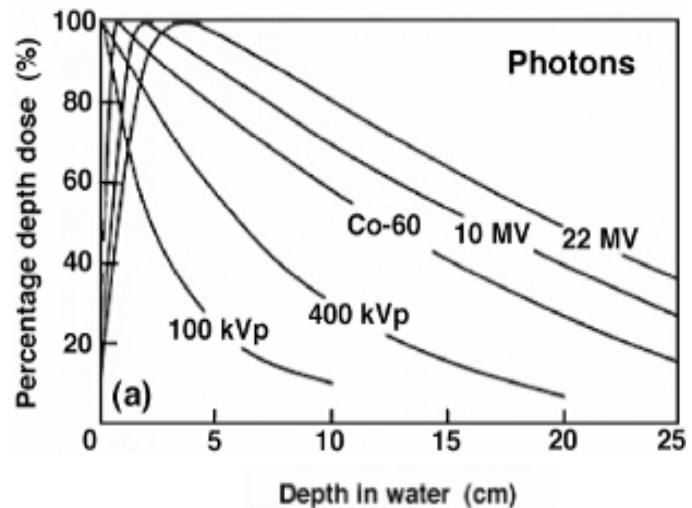
PDD is a key device performance consideration that may affect which type of device a researcher selects to conduct an experiment. Researchers must be able to accurately deliver specific doses of radiation to the target, regardless of depth. The radiation characteristics required for an experiment will therefore depend on the sample material (e.g., cells or animals) and the study point (e.g., internal organs, whole body, or epidermis). Because the PDD capabilities of irradiators depend on the energy spectrum of the radiation delivered, not all devices are able to deliver the required dose to a particular target with the same efficacy.

Due to the differential energy distributions of gamma and x-ray sources, the suitability of x-ray irradiators for medical research currently using cesium-137 is highly dependent on the specific research goals and requirements. Some research clearly requires a PDD that is only produced by radioisotope-based irradiators, while other research does not. It is unclear for many research applications whether x-ray technology could be a sufficient replacement, and few studies have been conducted to compare the results of irradiation from x-ray and radioisotope sources. There may also be instances in which an experiment can be altered to compensate for PDD limitations—such as specimen rotation in an x-ray device—but these methods may be challenging to execute or reproduce effectively.

A recent study undertaken at Mount Sinai Medical Center sought to determine whether a 160 kVp x-ray irradiator could be used instead of the cesium-137 devices (662 keV) normally employed for research using mice and cells.⁹⁵ The study identified a number of parameters on which the outcomes differed, but found that the relative biologic effectiveness (RBE) of the exposures was comparable. The authors also noted that the dose distribution resulting from x-rays with reflectors was more homogenous than that from the gamma devices without reflectors. A similar study was performed by researchers at Sandia National Laboratory and the Lovelace Respiratory Research Institute.⁹⁶ They assessed the replacement potential of 320 kVp x-rays for research that currently employs a cesium-137 device. In this case, the effectiveness of x-rays was shown to vary with cell type. Both studies noted that further such comparison studies are necessary and would aid researchers considering a transition from one technology to another. However, another study found significant differences in B, T, and myeloid cell reconstitution between x-ray and cesium-137 gamma irradiation for small animal tests after a period of 90 days.⁹⁷

Researchers often design experiments based on device availability, and then determine the dose endpoints achievable. However, they may not have the knowledge or information to support the adaptation of that dose requirement to different irradiator configurations (e.g., how the energy is being delivered or from how far

Figure 2.2: Energy distribution. (Courtesy of National Academy of Sciences)



⁹⁵ Mount Sinai, "Mount Sinai Experience in Migrating From Radioactive Irradiators to x-Ray Irradiators for Blood and Medical Research Applications," New York, September 2018, https://media.nti.org/documents/Mt_Sinai_Final_Report.pdf.

⁹⁶ Scott, B. R., K. M. Gott, and J. Wilder, "A Comparison of In Vivo Cellular Responses to Cs-137 Gamma Rays and 320-Kv X Rays," *Dose-Response*, 11: 444–459, 2013.

⁹⁷ Gibson, Brian W. et al., "Comparison of Cesium-137 and X-ray Irradiators by Using Bone Marrow Transplant Reconstitution in C57BL/6J Mice," *Comparative Medicine*, Vol 65, No 3, June 2015, pages 165–172.

away). Many researchers do not have the dosimetry expertise to measure doses with minimal uncertainties, therefore they do not have the knowledge of uncertainty analysis to accurately quantify the dose and biological endpoint uncertainties. This means that detailed analysis of this information is difficult to find and interpret in scientific publications, and unless researchers have access to each device they want to consider and the resources to analyze them, they cannot conduct their own comparison research. Researchers who are heavily dependent on long-term study protocols or historical data will have an even greater need for this comparison data to validate their experiment design with an alternate device. It is possible to provide correction factors for moving from a cesium-137 or cobalt-60 irradiator to an alternative technology, but most researchers reject this approach due to an inability to adequately assess and control the resulting uncertainties. This may hinder the adoption of alternative technologies in research applications. In some cases, switching to a new modality would reduce or eliminate the ability to compare the new research results and conclusions to those obtained through prior research efforts.

ASTM International has written a technical standard to address this issue. ISO/ASTM 51900 is being updated to deal with all research that requires proper dosimetry.⁹⁸ It covers the minimum requirements for dosimetry needed to conduct research on the effect of different products. In addition, x-ray irradiator manufacturers are offering more options (e.g., small dose areas, imaging) that have research advantages.

In 2017 and 2018, the University of California (UC) system created a Working Group to assess the feasibility of replacing the university system's CsCl self-shielded irradiators with x-ray devices under the DOE/NNSA CIRP. Based on technical conferences and examination of published papers and presentations, participants from the UC Working Group published a list of key technical points on irradiator replacement; they found that cesium irradiators can provide a surface dose of less than half the maximum dose, while lower-energy x-ray irradiators have a high surface dose. Higher-energy x-ray machines using appropriate filters permit decent penetration with low surface dose; these devices match the depth dose of cesium-137 in up to 4 centimeters (cm) of tissue. Low energy x-ray machines have lower dose penetration than their cesium-137 counterparts. X-ray irradiation is generally better than cesium for collimation owing to the ability to create an x-ray point source with thin sheets of lead; cesium sources cast a broad penumbra from the extended line source. In addition, different requirements for experiments may make it desirable to purchase different x-ray irradiators with varying capabilities. For example, throughput will be crucial to some experiments, requiring an x-ray with a comparable or higher throughput than a cesium machine. Lower-energy machines may be sufficient for some experiments while also being less expensive to purchase, install, operate, and maintain.⁹⁹

The UC Working Group also found that it is difficult to provide a simple conversion factor for equating x-ray effects with cesium-137 effects because RBE depends on multiple factors including x-ray peak energy, x-ray energy spectrum (filtration), details of the experimental set-up such as distance of the specimen from the source and the field size, biological system, endpoint, etc. Each experiment will need to be individually calibrated when converting from cesium irradiators to x-ray irradiators, and the effort and resources required will depend on the precision of the effect desired. In the case of feeder production or blood irradiation, the specificity of the absolute dose may not be as critical as ascertaining a tumoricidal dose or animal lethality dose; the RBE is more important for tumor models and radiobiology studies that may be more sensitive.

⁹⁸ "ISO/ASTM 51900 Guide for Dosimetry in Radiation Research on Food and Agricultural Products," International organization for Standardization (ISO), 2nd edition, June 2009, <https://www.iso.org/standard/44182.html>.

⁹⁹ MacKenzie, C. and K. Smith, "University of California System-Wide Plan to Replace Caesium Irradiators With Alternative Technologies," paper presented at the IAEA International Conference on the Security of Radioactive Material: The Way Forward for Prevention and Detection, 3-7 December 2018, Vienna, Austria IAEA-CN-269, available at https://media.nti.org/documents/Radioactive_Source_Replacement_Working_Group_Recommendations_05_02_18_FINAL.pdf.

Feeder-cell work and bone marrow work is generally less sensitive, since the final goal is to inactivate proliferating cells.

In 2016, biomedical researchers from two government agencies were surveyed for their perspective on switching from cesium or cobalt research irradiators to x-ray irradiators. This informal survey captured the responses of 25 users of cesium-137 irradiators and nine users of cobalt-60 irradiators. Responses showed that the researchers utilizing a cesium-137 irradiator primarily used it for irradiating feeder cells (50 percent) and/or for creating chimeric mouse models (32 percent), with a lesser number using it to irradiate human cell lines (20 percent), antigen-presenting cells (16 percent), tumor cells (8 percent), or other cells/organisms (12 percent). The majority of the cesium-137 irradiator users supported, or at least expressed a willingness to consider, a switch to x-ray: 10 of the 25 stated outright that switching to x-ray would not present a problem. An additional 13 cited for the need to confirm and re-optimize their experiment before they would feel comfortable switching to the new technology. Five cesium users stated outright that x-ray irradiation could not produce the result they needed, and three cesium users would not switch because they feared the introduction of a new variable in their experiments.

Researchers utilizing a cobalt-60 irradiator primarily used it for inactivation of biological specimens such as viruses and select agents. The majority of the cobalt-60 irradiator users (six) stated they could switch to x-ray, though some were reluctant to consider it due to the absolute need to validate experimental results first. The remaining 3 cobalt-60 users stated they could not switch due to the impracticality or infeasibility of the x-ray irradiator system for their work. Note that this survey provides anecdotal evidence only but does give a perspective on the wide range of research applications offered by cesium-137 and cobalt-60 irradiators, as well as on the varying degree to which governmental scientists feel confident in adopting replacement technology for their research.¹⁰⁰

DOE-NNSA Cesium Irradiator Replacement Program (CIRP)

Efforts to replace Category 1 and 2 radioactive sources with effective alternatives have become increasingly successful for research irradiation, in large part due to technological advances that have improved the reliability and cost of x-ray irradiation devices. Under its CIRP, DOE-NNSA offers cost-share support for Cs-137 device replacement (typically 50 percent of the new device cost). CIRP is entirely voluntary. Program participants are responsible for selecting the non-isotopic replacement device that meets their technical, operational, and financial requirements as well as for costs related to new device training and the purchase of a warranty or maintenance agreement for the new device, if applicable. CIRP support includes removal and disposal of the CsCl irradiator by NNSA/OSRP. Since the CIRP program inception in 2015, about 25 percent of the self-contained research irradiation devices used in the United States for a wide variety of research applications have been voluntarily replaced or are in the process of being replaced.

Radiation Source Protection and Security Task Force, Nuclear Regulatory Commission, *The 2018 Radiation Source Protection and Security Task Force Report*, (Washington, DC: 2014) page 22, Available at <https://www.nrc.gov/docs/ML1827/ML18276A155.pdf>.

¹⁰⁰ Interagency Working Group on Alternatives to High-Activity Radioactive Sources, *Transitioning from High-Activity Radioactive Sources to Non-Radioisotopic (Alternative) Technologies A Best Practices Guide for Federal Agencies*, (Washington, DC, 2016). Available at https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/ndrd-gars_best_practices_guide_final.pdf.

Administrative and Regulatory Requirements

Cesium-137 irradiators come with greater regulatory and licensing requirements than x-ray devices. In March 2013, the NRC published a final rule in the Federal Register to increase security requirements for the use and transport of risk-significant quantities of radioactive material, including the types of cesium-137 and cobalt-60 sources used for blood irradiation.¹⁰¹ The rule contains requirements for background investigations; access controls; security plans; immediate detection, assessment, and response to unauthorized access; tracking of shipments; security barriers; and other requirements. All licensees who possess subject radioactive material are under the current regulatory oversight of the NRC or applicable Agreement State.

Many facilities, especially hospitals, maintain institutional security for the protection of staff, patients, and information. However, similar to protection requirements for biological materials and controlled substances, the protection of radioactive materials requires additional security and costs. The NRC initially estimated that the average cost of implementation for licensees would be a one-time fee of approximately \$23,375 and an annual cost of approximately \$21,736 to fully implement the rule.¹⁰² However, licensees have reported varying cost estimates, both lower and higher. These costs depend on the number of individuals who are granted unescorted access to the device, the number of procedures that must be newly developed, the actual security measures that are used to meet the requirements, and the extent of training. Licensees have already been subject to these requirements for more than a decade, so may have compliant procedures and training already in place. The actual costs also depend on the number of sealed sources possessed by a licensee and the location of the sources relative to other sources and assets at the facility.

Additional costs include an annual program review and the maintenance and testing of security-related equipment. The review is important for licensees to evaluate the effectiveness of the program and to ensure that requirements are being implemented. Maintenance and testing ensure equipment is operational and available when needed.¹⁰³

Disposal Costs and Considerations for Sealed Source Irradiators

The proper disposal of radioactive materials used by the private sector is the responsibility of the licensees who benefit from them commercially. However, commercial disposal access challenges and security concerns related to high-activity sources has led to a temporary increase in government involvement, including the assumption of significant costs related to disposal.

Source Disposal

As indicated in federal legislation, the proper disposal of radioactive materials used by the private sector is the responsibility of the licensees who benefit from them commercially.¹⁰⁴ However, due to commercial disposal access challenges and security concerns, the Federal Government has recovered and disposed of

¹⁰¹ 10 C.F.R. Part 37, “Physical Protection of Byproduct Material” [NRC 2013f].

¹⁰² U.S. Nuclear Regulatory Commission, “Rulemaking Issue Affirmation: Final Rule: Physical Protection of Byproduct Material, (10 C.F.R. Parts 20, 30, 32, 33, 34, 35, 36, 37, 39, 51, 71, and 73),” (Washington, DC: December 2011).

¹⁰³ Ibid.

¹⁰⁴ Commercially generated radioactive waste in the United States (with the exception of spent fuel used in commercial power generation) is classified according to NRC regulations as Class A, B, C, or “greater-than-Class C” (GTCC) low-level radioactive waste (LLRW), depending on its radioactivity concentration and half-life. The Low-Level Radioactive Waste Policy Amendments Act of 1985 (LLRWPA) makes States responsible for providing disposal options for Class A, B, and C LLRW generated within their borders, while DOE is responsible for providing disposal options for Greater-than-Class C (GTCC) LLRW, including the implementation of mechanisms to ensure that the commercial entities who benefit financially from the activities resulting in GTCC waste generation will bear reasonable costs for its disposal.

tens of thousands of disused and unwanted Category 1 and 2 sources across the past 20 years at no cost to users.¹⁰⁵ This has included cesium-137 and cobalt-60 gamma irradiation devices, which remain highly radioactive even after the source material has decayed to the point that the device is no longer effective for the user.

Recently updated NRC disposal guidance enables radioactive material licensees to dispose of many Category 2 cesium-137 sources at currently operational commercial radioactive waste disposal facilities.¹⁰⁶ This likely includes cesium-137 irradiator sources up to the ~957Ci Class C limit for the material. The guidance also enables commercial disposal of most or all Category 1 and 2 cobalt-60 sources as Class A or B waste due to their short half-life. In addition, DOE has made significant progress toward establishing a disposal pathway for GTCC waste, including the highest activity cesium-137 sources used in blood and research irradiators.

As commercial disposal options for Category 1 and 2 sources become increasingly available, access to subsidized disposal may be limited. As a result, significant gamma irradiator lifecycle costs will shift back to commercial users. Although the ultimate cost structure that will apply to GTCC sources remains uncertain, disposal fees for Class A, B, and C waste at currently operational commercial disposal facilities are based primarily on the volume and Ci of the waste.

Recycle

Some irradiator manufacturers will accept return of cobalt-60 of their own devices for source recycling. This reduces environmental and cost impacts of disposal, but usually at additional cost to the licensee.

¹⁰⁵ Pending the availability of commercial disposal options, the National Nuclear Security Administration (NNSA)/Off-Site Source Recovery Project (OSRP) recovers and disposes of high-activity sources in the interest of National security, public health, and safety at Federal facilities primarily intended for the disposal of waste generated by the U.S. government. These sites operate under different legislative authorities than commercial disposal facilities and are prohibited from accepting waste, including sealed sources, directly from commercial radioactive waste generators. Commercial radioactive material licensees may register their sources with NNSA/OSRP, which prioritizes them for recovery according to criteria determined in consultation with the NRC.

¹⁰⁶ U.S. Nuclear Regulatory Commission. "Concentration Averaging and Encapsulation Branch Technical Position, Revision 1," Volumes 1 and 2. February 2015. (ADAMS Accession No. ML12254B065).

Chapter 3: Alternative Technologies for Radiotherapy

Introduction

Radiation therapy is an essential tool in the curative and palliative care for many types of cancer. Approximately 60 percent of patients with cancer diagnosis will receive either external or internal radiotherapy at some point during their treatment. External radiotherapy involves the application of ionizing radiation emitted from a device outside of the patient to treat the disease location. External radiotherapy devices include stereotactic radiosurgery (SRS) devices used primarily to treat tumors in the head and neck, and teletherapy devices used to treat cancers throughout the body. Radioisotopic devices for these applications use Category 1 quantities of cobalt-60. In the United States, non-radioisotopic e-beam accelerators have largely supplanted the use of the cobalt-60 devices for teletherapy applications. However, many SRS devices still use cobalt-60.

Internal radiotherapy, called brachytherapy, involves temporary or permanent placement of a small radiation source, often called a “seed,” of radioactive material into the patient at or near the cancer location. These sources individually do not typically exceed Category 2 thresholds; as result, these applications are not considered in this report. This chapter will focus on external beam radiotherapy applications.

Commercially Available Radiotherapy Technology—Isotopic and Alternatives

In its consideration of the external radiotherapy applications addressed in this chapter, the ATWG noted that use and replacement considerations for these devices vary significantly among regions and nations.¹⁰⁷ In general, resource-limited environments often must prioritize factors that may be of secondary importance in a domestic context. In addition to the capital investment required for a device, additional factors may include reduced access to maintenance or training resources for more complex devices, a less stable power grid, and the operational flexibility to treat a wider range of patients with fewer devices. These and other factors have led to the more-common use of certain lower cost cobalt-60 devices internationally than in the United States. While these are important issues from a both a public health and non-proliferation standpoint, they are beyond the scope of this chapter. The focus here, as in the rest of this report, is on device use and potential replacement in the United States.

Patient care decisions rely on the knowledge, expertise, and experience of medical care provider(s) and may differ for each individual medical treatment, resulting in divergent medical opinions on the effectiveness of various ionizing radiation treatment options compared with alternatives. As a result, this chapter attempts to remain neutral, seeking to provide helpful information without advocating for specific treatment options.

¹⁰⁷ See, for example, Atun, Rifat, et al. 2015. “Expanding Global Access to Radiotherapy,” *The Lancet Oncology* 16 (2015): 1153-86.

Teletherapy

The two types of devices most commonly used for teletherapy are gamma devices that use relatively high energy and high-activity radioactive cobalt-60 sources and linacs that generate high-energy x-rays. Linacs use high-powered electro-magnetic fields to accelerate electrons at target made of dense material.¹⁰⁸ The resulting collision produces high-energy x-rays that are particularly effective for the treatment of deep-seated tumors. Both technologies use ionizing photon radiation to destroy tumor cells embedded within the patient.

The e-beam radiation produced by linacs may also be used to treat diseased cells on or near the surface. Proton therapy, which also uses accelerator technology, may also be used in some cases for external beam cancer treatment. There are presently 27 proton beam units in the United States, with another 20 under construction or development. However, e-beam and proton therapy are more specialized and much more expensive treatment options when compared with gamma or x-ray treatment—a distinction that is not expected to change as the technologies continue to evolve in the near- to mid-term. Therefore, proton therapy is not treated in this chapter as a replacement technology for cobalt-60 and linac devices.

Cobalt-60 devices and linacs emerged in the 1950s as rival technologies; cobalt teletherapy quickly became the most widespread form of external beam therapy, primarily due to the superior safety, reliability, precision, and simplicity of the devices relative to linac technologies at that time. By the late 1960s, approximately 90 percent of the 1,700 external beam devices in the world were cobalt units. In the 1970s and 1980s, however, the use of linacs increased significantly due to technological advances in the devices. Improved accelerator technologies reduced the space and power requirements of the otherwise large and energy-intensive devices, while improved filter and foil technology enabled the production of flatter, more effective e-beams.¹⁰⁹ A clinical consensus also considered linac treatments superior to cobalt-60 treatments for cancers of the breast, head, and neck. By the late 1980s, device preferences had reversed, with more than 90 percent of teletherapy units in the United States using linac technologies. The sharpness of the beam edge of a linac compared with the larger penumbra of cobalt-60 due to the source and spot size, as well as the much higher radiation dose-rate of the linac, make it suitable for complex focal treatments now used in radiation therapy. With the advent of computer-based treatment planning, treatments now generally use three-dimensional (computed tomography [CT]-based) rather than the two-dimensional systems (planar films) previously employed. The move from two-dimensional to three-dimensional treatment planning (for both linac and cobalt-60 units) is becoming a goal of this type of care worldwide.

Although the predominance of linacs for teletherapy continues, technological advances in certain devices that use cobalt-60 sources have more recently led to a resurgence in the use of cobalt-60. These advances include the use of multiple sources fitted with multi-leaf collimators (MLCs) in standard teletherapy units, radiation beam modulation for more precise radiation targeting, and the addition of digital user interface technologies.¹¹⁰ Specialized radiosurgery devices in the United States that use a large number of relatively small cobalt-60 sources for treatment of malignant and benign brain tumors, vascular malformations, and functional disorders are utilized given the desired outcomes, advocacy by physicians, and workflow. However, linac and similar devices may also provide effective treatment options for the same medical ailments.

¹⁰⁸ Typically, materials with high Z numbers (protons) and therefore a large number of orbiting electrons that can produce bremsstrahlung radiation. Examples of such material include, but are not limited to, lead and tungsten.

¹⁰⁹ Hogstrom, Kenneth and Peter Almond. 2006. "Review of Electron Beam Therapy Physics." *Physics in Medicine and Biology* 51: R455-R489.

¹¹⁰ Fox, Christopher H., Edwin Romeijn, Bart Lynch, Chunhua Men, Dionne M Aleman, and James F Dempsey. 2008. "Comparative Analysis of ⁶⁰Co Intensity-Modulated Radiation Therapy," *Physics in Medicine and Biology*. 53: 3175-3188.

Teletherapy treatments are usually fractionated—that is, the total dose is delivered across several weeks of treatment sessions. The amount of dose delivered per session is typically 180 to 200 centigray (cGy).¹¹¹ The total dose for the entire treatment can vary from 3,000 cGy to 8,000 cGy. The treatment technique may deliver the entire dose at one angle, at multiple angles, or in a continuous sweep around the patient, depending on the machine capabilities and treatment requirements. Recently there has been a shift toward shorter courses of radiation using fewer, higher-dose fractions; this is called hypofractionation. Hypofractionation is made possible due to improvements in imaging, computerized treatment planning, computer control of the linac, and image guidance during the treatment. These capabilities increase versatility and often desirability by radiation oncologists but also add substantial expense.

To summarize, the primary challenge for radiation oncologists planning teletherapy treatments is to effectively target diseased cells while sparing healthy surrounding tissues. Technological advances in both gamma and linac devices, advances in computerized planning, and on-board imaging have increased practitioners' ability to do this successfully.

Teletherapy device purchase decisions involve a wide range of factors. In developing countries, where infrastructure and training are often a challenge, a facility's ability to operate and maintain a device often takes precedence. In the United States, training and infrastructure are not typically a significant challenge. United States device selection primarily involves considering the range and types of treatment the purchaser expects to provide, the clinical experience and preferences of the practitioners, and the costs associated with the purchase and use of the devices.

General Purpose Teletherapy Devices

Cobalt-60

There are currently approximately 15 teletherapy devices in the United States that use cobalt-60.¹¹² Standard cobalt-60 teletherapy devices use a single source to deliver the required radiation dose to the patient. The average gamma/photon energy of cobalt-60 is 1.25 MeV. Dose rates at 80 cm isocenter typically vary from 100 to nearly 400 cGy per minute (cGy/min), depending on the current activity of the source.¹¹³ A typical unit consists of the following:

- Control console
- Treatment couch
- Treatment head that includes the following:
 - cobalt-60 radiation source
 - Source housing and shielding material
 - Aperture for the exposed source
 - Mechanism to move the source toward or away from the aperture
- Gantry assembly that moves the treatment head relative to the patient

¹¹¹ 100 centigray = 1 Gray.

¹¹² Includes devices for both human and veterinary medical applications. Data provided by the NNSA Office of Radiological Security. This figure does not include Co-60 SRS devices, which are considered separately below.

¹¹³ BT GB100-80 and Equinox are 15,000 Ci and 390 cGy/min. "Technical Specifications," Best Theratronics, Accessed march 21, 2019, http://www.theratronics.ca/PDFs/BT_GB_100-80_tech_specs.pdf.

The cobalt-60 sources used in the devices have an initial activity of 5,000 to 15,000 Ci, but must be replaced every five to seven years due to the 5.27-year half-life of the material. The relatively rapid decay of the material—about 1.1 percent per month—requires clinicians to regularly assess and adjust treatment times accordingly. As the cobalt-60 source ages, the time for each treatment lengthens due to reduced gamma emissions of the radioisotope, which can impact the throughput of treatment facilities already at capacity.

Teletherapy source capsules are typically 2 to 3 cm in length, with a diameter of 1 to 2 cm. Due to their size and shape, these sources produce a relatively large uniform beam at the center of the field with significant dose profile variation between the center and the edges of the field. The rectangular field size can range in length from about 5 cm up to about 35 cm. Variations in the dose profile are a challenge from a treatment perspective because they make it more difficult to deliver the intended dose to a target area without also damaging healthy, non-target areas.



To facilitate the production and use of both the sources and the devices, standard cobalt-60 teletherapy source capsules, with a height of 2.5 cm and active diameters typically ranging from 1 to 2 cm have been developed. The smaller source diameters reduce the penumbra—the dose profile variation caused by source geometry—but are more expensive. Often a diameter of 1.5 cm is chosen as a compromise between the cost and clinical limitations.¹¹⁴ To mitigate the penumbra effect in standard devices, shielding material or other simple collimators can be placed between the source and the patient. Some shielding material can be molded using patient x-rays and can also shape the radiation field to more closely conform to the target area.

The simplicity of standard cobalt units may provide certain advantages relative to linacs, particularly for users in less-developed countries that may lack the technical training or infrastructure stability required for more complex devices. These advantages include reduced operational and maintenance costs and limited downtime. There are, however, some disadvantages to cobalt-60 units compared with linacs. For instance, treatments using simple cobalt-60 units are limited to relatively simple techniques, reducing their treatment scope and efficacy.¹¹⁵ Further disadvantages of these devices compared with linacs include the following:¹¹⁶

- A relatively large penumbra effect resulting in unwanted radiation to healthy organs and tissues (including the skin);
- Limited dose penetration, making it more difficult to treat deep-seated tumors;

¹¹⁴ Podgorsak, E.B., *Radiation Oncology Physics: A Handbook for Teachers and Students*, (Vienna: International Atomic Energy Agency: 2005).

¹¹⁵ "Debate," *Journal of Cancer Research and Therapeutics*, 2014, 10:781-90.

¹¹⁶ "Debate," *Journal of Cancer Research and Therapeutics*, 2014, 10:781-90; Fox, Christopher H., Edwin Romeijn, Bart Lynch, Chunhua Men, Dionne M Aleman, and James F Dempsey, "Comparative Analysis of Co Intensity-Modulated Radiation Therapy," *Physics in Medicine and Biology*. 2008, 53: 3175-3188.

- Relatively low dose rate (maximum 250 cGy/min);
- Source decay of approximately 1 percent per month (12 percent per year), which requires prolonged treatment times and source replacement; and
- Radioactive material-related challenges, including safety and security regulatory compliance.

The cobalt-60 teletherapy units still in use in the United States employ technological advances initially developed for the linac to counter the disadvantages of standard cobalt-60 devices. Sophisticated computer software, three-dimensional imaging, and advanced MLCs enable practitioners to shape the gamma beam to more precisely conform to the tumor profile. Intensity-modulated radiotherapy (IMRT) can further improve radiation delivery by varying beam intensity to more tightly conform to the shape of the tumor. Newer device models may use multiple sources to even more precisely target dose delivery and to increase dose rate capabilities. However, multiple cobalt-60 source beam treatments can also be replaced, in some cases by linacs that incorporate magnetic resonance guidance capabilities.¹¹⁷ For example, the ViewRay MRIdian® contains three sources with a combined original activity of 45,000 Ci. The sources provide a dose rate of 600 cGy/min or more. As of 2017, there were approximately four MRIdian® units in use in the United States.¹¹⁸ However, two have recently been replaced with linac devices. The MRIdian® devices typically weigh approximately 10,000 lbs including the treatment table and require about 35 square feet of floor space.

Linear Accelerators

Linacs use high-powered electromagnetic fields to accelerate electrons aimed at a tungsten (or similar-material) target. The resulting collision produces high-energy x-rays that are particularly effective for the treatment of deep-seated tumors. The peak photon energy of these devices is the same as or substantially higher than that produced by cobalt-60, typically varying from 4 to 25 megavolts (MV) or higher depending on machine specifications.¹¹⁹ The average photon energy, however, is only a third of peak energy. In linacs that produce 6 MV or higher energies, the electrons can also be diverted prior to x-ray generation for the treatment of diseased tissues on or just below the skin surface. A typical linac will provide 6 and 18 MV x-ray beams and several electron energies between 4 and 22 MeV.¹²⁰ However, with the trend toward image-guided radiation therapy, some of the newer linacs produce single energy around 6 MV. Linacs use a flattening filter and MLCs to shape the scattered photon energy to the appropriate beam shape and uniformity at the desired depth. Multiple exposure and timing systems help ensure the accuracy of the dose delivered.

Linacs are mounted such that they always focus on a single point (isocentrically) and the operational systems are distributed across five major and distinct sections of the machine:¹²¹

- Gantry
- Gantry stand and support

¹¹⁷ Elekta Corporate, “Why MR/RT?” Website, accessed May 3, 2018, <https://mrrt.elekta.com>.

¹¹⁸ ViewRay, Inc., Form 10-K Annual Report, Securities and Exchange Commission, filed March 17, 2017, <http://phx.corporate-ir.net/phoenix.zhtml?c=253882&p=irol-sec>.

¹¹⁹ The unit MV refers to “megavoltage peak.” It describes the accelerating voltage of the accelerator, the resulting energy of accelerated electrons, and the maximum energy of any generated x-rays. As an example, a 6 MV linac produces x-rays of a broad energy spectrum up to 6 MeV with an average energy around 2 MeV. For a discussion of x-ray generation, see Chapter 2.

¹²⁰ Podgorsak, E. B., *Radiation Oncology Physics: A Handbook for Teachers and Students*, (Vienna: International Atomic Energy Agency: 2005), 273.

¹²¹ Podgorsak, E.B. “Chapter 5: Treatment Machines for External Beam Radiotherapy,” presentation based on the IAEA publication *Radiation Oncology Physics: A Handbook for Teachers and Students* by E.B. Podgorsak, (ISBN 92-0-107304-6), Version 2012.

- Modulator cabinet
- Patient support assembly
- Control console

The main beam-forming components of a modern medical linac include:

- Injection system
- Radiofrequency power generation system
- Accelerating waveguide
- Auxiliary system
- Beam transport system
- Beam collimation and monitoring system

Advanced linac treatment heads are composed of several components:

- Several retractable x-ray targets (one for each x-ray beam energy)
- Flattening filters (one for each x-ray beam energy)
- Scattering foils for production of clinical e-beams
- Primary collimator
- Adjustable secondary collimator with independent jaw motion
- Dual-transmission ionization chamber
- Field-defining light and range finder
- Retractable wedges
- MLCs

However, there are significant variations from one commercial machine to another, depending on the e-beam energy and the particular design used by the manufacturer.¹²² Advanced linacs include treatment planning systems that enable imaging in the treatment position. These images allow physicians to see and contour the tumor volume. MLCs and image-guiding technologies also enable the treatment of patients with IMRT and allow for image-guided radiation therapy (IGRT). In IMRT, the MLCs move during beam application, enabling increased dose to the target and less to the nearby normal tissue. In addition, newer image-guiding techniques such as volumetric arc therapy (VMAT) can shorten treatment times but depend on highly skilled support staff.

Higher-energy linacs are also known to produce neutrons via photonuclear reaction. Sufficiently high-energy photons (>10 MeV) have been known to interact with heavier nuclei, such as the zinc found in medical linacs, and cause neutrons to be emitted. The nuclei may themselves become radioactive and decay, producing additional radiation. The neutrons produced by the photonuclear reactions can result in unintended exposure to patients and staff, either directly or through neutron activation of surrounding material. Proper shielding should be in place at facilities with higher-energy linacs to protect against this neutron radiation.

Due to their complexity, linacs require staff to regularly perform quality assurance checks, machine calibration, and routine maintenance. Linac device components include vacuum pumping systems, water cooling systems, air pressure systems, beam transport systems, drift tubes, bending magnets, steering coils, focusing coils, and dual-transmission ionization chambers. Linacs also require significant and stable

¹²² Podgorsak, E. B., *Radiation Oncology Physics: A Handbook for Teachers and Students* (Vienna: International Atomic Energy Agency: 2005).

electrical power for operation, including 250 volts (V)/150 amperes (A) for beam generation, as well as 480 V/30-60A for cooling systems and other components.¹²³ Additionally, linacs increasingly rely on multiple, networked computer systems, making network stability critical. If a hospital network is down, the corresponding linac is typically unable to operate.

Stereotactic Radiosurgery Devices

Stereotactic radiosurgery (SRS) precisely directs radiation in three dimensions to a target area within the head or body using coordinates provided by medical imaging. In contrast to conventional radiotherapy, radiosurgery treatments usually deliver the required dose in a single exposure instead of fractionating the prescribed dose over multiple treatment sessions. In general, the use of SRS and hypofractionation based on the physical ability to shape the beam and avoid normal tissue is increasing. Short- and medium-term results support this use in a number of disease sites, but careful studies of long-term effects are essential for assessing its impact. Since long-term effects are not a concern for palliative radiation therapy, the reduction in the number of treatments and overall treatment time are important for patient comfort and in resource-limited settings.

Both linacs and cobalt-60 devices can be used for SRS treatment. For some applications, particularly tumors located in the brain, either radiation source may be used for treatment, with varying clinician preference, but this may not be true for all treatments and types of tumors. SRS devices require significant supporting infrastructure, with estimated costs of approximately \$2 million for construction.¹²⁴ As a result, the upfront cost of an SRS device, irrespective of radiation source type, is roughly \$4 million, plus annual maintenance costs of about \$300,000.

Cobalt-60 Devices

There are approximately 120 cobalt-60 SRS devices in service in the United States, used primarily to treat brain tumors and skull-based lesions. The Elekta Gamma Knife® is the most common of these devices and is used for head treatments. The Gamma Knife's various models use between 192 and 201 cobalt-60 sources of 30 Ci each. American Radiosurgery sells an SRS device that is less commonly used and utilizes 30 sources of 200 Ci each. While the gamma beams from the individual sources in these devices are not strong enough to significantly damage healthy tissues, their convergence at the target location provides the high dose needed for treatment. New units deliver approximately 350 cGy/min, but the dose rates vary due to the relatively short 5.27-year half-life of the cobalt-60. The sources are often replaced every few years to minimize the dose-rate variation.

Most of the time, treatment planning occurs the same day as computed tomography (CT) imaging and magnetic resonance imaging (MRI). Highly precise, image-based beams are enabled by multiple, complex collimators that focus the beams on the target location. A head frame attached to the patient facilitates precise setup, localization, and dose delivery, while the treatment table moves the patient to the appropriate

¹²³ The availability of reliable three-phase power still must be confirmed; for example, a linear accelerator requires a 250 V/150 A power supply, a chiller requires 480 V/60 A, an air-conditioning plant requires 480 V/30 A, and a conventional simulator requires 480 V/60 A. See International Atomic Energy Agency, *IAEA Human Health Report No. 10: Radiotherapy Facilities: Master Planning and Concept Design Considerations* (Vienna: International Atomic Energy Agency: 2014).

¹²⁴ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008), 132.

position for treatment. The utilization of Gamma Knife by center can vary widely, with most centers able to treat two to three patients per day.

Linac Devices

There are several manufacturers of linac SRS treatment devices, including Accuray and Varian. The Accuray CyberKnife is used in approximately 150 treatment centers nationwide¹²⁵ for both head and body treatments. The CyberKnife was first approved for clinical use in 2001 and uses 6 MV linacs mounted on a robotic arm with six degrees of translational and rotational freedom. These devices rely on image-guidance technologies for highly conformal photon-beam application, automatically correcting for target movement during treatment. These capabilities make the use of a patient frame for head and neck treatments unnecessary. With the addition of an MLC and image guidance, linacs are also used for SRS and radiotherapy throughout the body. Common applications include treatment of spine, lung, and prostate cancers, often using hypofractionation. Varian Medical Systems markets the TrueBeam and Edge devices with capabilities similar to those of the CyberKnife.

The following section outlines considerations on which potential buyers may base their purchase or replacement decisions, including a device's ability to meet site and application requirements, cost, and security factors of each technology.

Lifecycle Technology Costs

Radiotherapy and Stereotactic Radiosurgery Device Cost Comparison

Radiotherapy costs can be divided into two primary types. Upfront costs involve establishing a new facility, including the cost of the facility and device and staff training. Ongoing costs start once the facility is operational and include power consumption, maintenance, downtime, and source replacement. Both upfront and operational costs vary depending upon a variety of factors, including facility construction, training requirements, equipment type, level of treatment complexity, and patient throughput.¹²⁶ Regardless, the technical advantages supplied by linac teletherapy units over cobalt-60 devices generally come at a significantly increased financial cost.

Due to the lack of publicly available price information and the wide range of device types and cost variables, a true cost-comparison of linac and cobalt-60 devices is beyond the scope of this group to develop. In addition, the purchase price of a single device can vary among purchasers and across time due to business factors, such as customer relationships or changes in the availability of competing devices. Operational costs, such as maintenance contracts and source reloading for gamma devices, may also vary due to similar business considerations. Although this chapter attempts to include the best available information and tries to identify cost factors that likely remain static over time, actual device purchase and use costs are likely to vary widely.

As depicted in Table 3.1: Teletherapy Device Cost Considerations below, the purchase price of linac devices generally increases with their energy output and is roughly three or more times the amount of the cobalt-60 devices currently in service. In the United States, there is a clear trend toward increasingly sophisticated and

¹²⁵ "Cyberknife Locations," CyberKnife, accessed January 27, 2017, <http://www.cyberknife.com/cyberknifelocations.aspx>.

¹²⁶ Atun, Rifat, et al., "Expanding Global Access to Radiotherapy" *The Lancet Oncology Commission* 2015, 16: 1153-86.

more capable radiation therapy. For both linac and cobalt-60 devices, the purchase price of the newer, more advanced models is much higher than older or more basic devices. For example, although their market share remains limited, devices that combine imaging and therapy, such as the MR-linac, are substantially higher in cost than the less sophisticated devices (by one estimate, as high as \$9 million). In addition, the distribution of costs across the device lifecycle is different for cobalt-60 and linac devices. Planned and unplanned device maintenance costs are likely substantially higher for linacs than for cobalt-60 devices, although more recent sources indicate that technological and maintenance process improvements have reduced the number and duration of unplanned linac downtime events.¹²⁷

Table 3.1: Teletherapy Device Cost Considerations¹²⁸

	Cobalt-60 Device	Low-Energy Linac (6 MV)	High-Energy Linac (18 MV and 5 electron energies)
Capital cost	\$750,000	\$2,250,000	\$4,000,000
Equipment maintenance and servicing	\$30,000/year	\$150,000/year	\$300,000/year
Cost of source replacement (every 5 years)	\$100,000	N/A	N/A
Device calibration downtime	Every 6 months	Twice per week	Twice per week

The primary operating costs of cobalt-60 units include source replacement every 5 years and end-of-life device decommissioning. The price of replacement sources varies based on the size, total activity, and design of the source, as well as on the prevailing supply and demand of cobalt-60. According to a 2008 estimate, the sources used in standard units cost approximately \$8/Ci, with source replacement costing about \$100,000.¹²⁹ Teletherapy device manufacturers typically offer source-exchange services for their devices, using device-specific containers to facilitate removal of decayed sources and installation of replacement capsules. While manufacturers may take possession of the removed source or sources following a 5-year source-exchange, disposing of the device at the end of its lifecycle may become costly due to reduced federal support for device disposal as commercial disposal options become increasingly available. Cobalt-60 device users may need to pay tens or hundreds of thousands of dollars more than in the past, depending on the availability of transportation containers and the cost calculation used by the disposal facility.

For SRS devices, the lifecycle costs are likely more similar across devices. However, it is difficult to provide a direct price comparison because the Gamma Knife is limited to cranial treatments, whereas linac SRS devices may also be used to treat areas throughout the patient. Table 3.2 identifies several primary cost considerations.

¹²⁷ Hoisak, Jeremy D. P., Todd Pawlicki, Gwe-Ya Kim, Richard Fletcher, and Kevin L. Moore. 2014. "Improving linear accelerator service response with a real-time electronic event reporting system." *Journal of Applied Clinical Medical Physics* 15(5): 4807.

¹²⁸ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008), 124.

¹²⁹ Ibid. and 26.

Table 3.2: SRS Device Cost Considerations¹³⁰

	Gamma Knife	CyberKnife/Linac
Equipment purchase cost	\$4,000,000	\$4,000,000
Annual service charge	\$320,000	\$320,000
Radiation source reload	\$1,000,000	N/A
Manufacturers estimated useful life (years)	15	10

The likely need for building, or “bunker,” shielding upgrades for a higher-energy linac device adds additional cost to gamma teletherapy or SRS device replacement. Since the penetrability of radiation is positively correlated with its energy level, replacement of a cobalt-60 device with a linac typically requires additional wall shielding. Less-expensive, standard concrete can be used when the additional thickness is not a design concern; however, facilities concerned with device mobility or spatial considerations may need to purchase more expensive shielding materials (e.g., high-density concrete or steel).¹³¹ Some SRS devices (such as the CyberKnife) require a minimum ceiling height of 12 feet, which adds more spatial and cost considerations.¹³² Linacs of sufficiently high energy may also require neutron shielding in addition to the tradition shielding used for beta and gamma radiation. Neutron shields are made of different materials than those used to protect against beta and gamma radiation, and some impurities found in concrete and steel may be undesirable for use in a neutron field due to activation issues. Special consideration must also be given to shield geometry and layering when considering neutron radiation. The takeaway for decision-makers is that installing a higher energy linac and the associated shielding may not always be as simple as adding more lead and concrete.

Gamma Knife source replacement is highly complex and expensive relative to standard cobalt-60 teletherapy unit replacements. By one estimate, replacement sources cost approximately \$160/Ci, due to their design specifications. However, the assessment also notes that prices may vary depending on a wide range of business factors.¹³³ The entire source reloading process can take 3 to 4 weeks and the total price for source exchange can approach \$1 million, depending on the device location and logistics.

Cobalt-60 Supply and Price Constraints

Gamma radiosurgery and teletherapy device production and use depend on a steady supply of encapsulated cobalt-60.

Recently the Idaho National Laboratory (INL) Advanced Test Reactor resumed production of high specific-activity (HSA) cobalt-60 used in medical devices. The initial shipments from INL are expected in early 2019.

¹³⁰ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008), 124.

¹³¹ International Atomic Energy Agency, “Radiation Protection in Radiotherapy, Part 7: Design of Facilities and Shielding, Lecture 2: Shielding,” IAEA Training Material on Radiation Protection in Radiotherapy, accessed January 27, 2017.
https://rpop.iaea.org/RPOP/RPoP/Content/AdditionalResources/Training/1_TrainingMaterial/Radiotherapy.htm.

¹³² ICF Incorporated, “Cost-Benefit Analysis for Potential Alternative Technologies for Category 1 and 2 Radioactive Sources,” U.S. Nuclear Regulatory Commission, Contract No. NRC-02-05-002, Task Order No. 5 (2009).

¹³³ Schlesinger, David, “Historical and Technical Overview of Gamma Knife Radiosurgery,” AAPM Summer School (Burlington, VT), 2014, <https://www.aapm.org/meetings/2014SS/documents/SU05SchlesingerFINALforHandouts.pdf>; Griffiths, Alison, Luke Marinovich, Michael B. Barton, and Sarah J. Lord, “Cost analysis of Gamma Knife stereotactic radiosurgery,” *International Journal of Technology Assessment in Health Care*, 2007, 23(4): 488-494.

United States medical source manufacturer International Isotopes Inc. has contracted with INL to purchase the entire INL supply of cobalt-60 under a 10-year supply contract. The contract stipulates annual shipment amounts, along with an annual 5 percent price increase.¹³⁴

Device Ability to Meet Site and Application Requirements

For teletherapy, medical practitioners generally recognize several advantages of linac devices relative to cobalt-60 devices for many types of treatment.¹³⁵ Table 3.3 indicates linacs' ability to deliver doses at greater depth than cobalt-60 while minimizing damage to surface tissues. The higher-energy photons produced by linacs are more effective for treating deep-seated tumors relative to the lower-energy photons produced by cobalt-60. Furthermore, rapidly emerging trends including IGRT, VMAT and hypofractionation will have a major impact on curative and palliative treatments, enabling shorter courses of treatment. However, as part of a range of treatments, the technologies may be clinically comparable.¹³⁶

Table 3.3: Approximate Dose-Depth Profiles for Common Photon Energies¹³⁷

Device Type	Photon Beam Energy	Approximate depth (cm) where dose is		
		Maximum	80% of max	50% of max
Cobalt-60	~1.25 MeV	0.5	4.7	11.6
Linac	4 MVp	1.0	5.6	13.0
	6 MVp	1.2	6.8	15.6
	10 MVp	2.0	7.8	19.0
	25 MVp	3.0	10.2	21.8

In addition, linac beam radiation generally has a more uniform dose profile compared with that produced by cobalt-60 devices, enabling more precise tumor targeting within surrounding healthy tissues. The linac also provides a relatively uniform dose rate throughout its service life, while the dose rate of cobalt-60 devices decreases across time due to radioactive material decay. As the dose rate of cobalt-60 devices decreases, patient treatment times must increase correspondingly. This reduces treatment capacity for the device. Table 3.4 presents a comparison of physical and other parameters for radiation sources of photon beams.

¹³⁴ International Isotopes Inc., "2017 Securities and Exchange Commission Form 10-K Annual Report," filed March 30, 2018, page F-19.

¹³⁵ Page, Brandi R., Alana D. Hudson, Derek W. Brown, Adam C. Shulman, May Abdel-Wahab, Brandon J. Fisher, and Shilpen Patel "Cobalt, Linac, or Other: What Is the Best Solution for Radiation Therapy in Developing Countries?" *International Journal of Radiation Oncology, Biology, Physics*, 2014, 89(3): 476-480.

¹³⁶ Dineley, Jude, "MR-guided cobalt-60 system measures up," *Medical Physics Web*, 2015.

¹³⁷ Adapted from the University of Vermont Department of Surgery, "Orthovoltage vs. megavoltage x-rays," accessed January 27, 2017.

<http://docplayer.net/20861999-1-orthovoltage-vs-megavoltage-x-rays-al-external-beam-radiation-sources-orthovoltage-radiotherapy-200-500-kv-range.html>.

Table 3.4: Comparison Physical and Other Parameters for Radiation Sources of Photon Beams¹³⁸

	Cobalt-60	Low-Energy Linacs (6 MV)	High-Energy Linacs (15 -18 MV)
Average photon energy	1.25 MeV	~2 MeV	~5-6 MeV
Depth of maximum dose	5 mm	15 mm	28-35 mm
Skin dose	40-50%	~25%	~15-25%
Percentage Depth Dose at 10 cm	54%	67%	77%
Shape of isodose curves	Rounded beyond central zone (correctable)	Flattened with special filter	Flattened with special filter
Integral dose/tumor dose ratio	More for non-optimal plans. Manageable with good plans	Less with simple fields	Less with simple fields
Beam collimation in asymmetric collimators	MLC being tried	MLC, IMRT, SRT/Stereotactic Body Radiation Therapy (SBRT)	MLC, IMRT
Irregular fields	Achievable with blocks. MLC in Viewray and Equinox™ only	MLC, mini-MLC (for small fields)	MLC
Computerized control console	Yes	Yes	Yes
Dose rate	~250 cGy/min	~300-600 cGy/min	400-600 cGy/min

Administrative and Regulatory Costs

Device Competency: Education, Training, Certification, and Standards

Despite the increased treatment options of linacs relative to newer cobalt-60 teletherapy and SRS models, linacs are more complicated to maintain and operate. Machine calibration is more frequent and rigorous, and the changes required are less predictable. As a result, safe and effective use of linac devices generally involves more extensive training than training for the simpler and more predictable gamma units.¹³⁹ Training and certification requirements for linac use are determined by state regulatory agencies. The NRC sets training and certification requirements for physicians who use cobalt-60 devices, including annual instruction in radiation protection and emergency procedures.

Regulatory Controls

The security of cobalt-60 teletherapy and SRS devices, both Category 1 sources, falls under the same NRC and Agreement State security requirements as the security of cesium-137 blood and research irradiators described in Chapters 1 and 2. Additionally, the use of gamma teletherapy and SRS units is regulated by the NRC and the Agreement States under Title 10, C.F.R. Part 35, Subpart H, “Photon Emitting Remote Afterloader Units, Teletherapy Units, and Gamma Stereotactic Radiosurgery Units” and corresponding State

¹³⁸ Ravichandran, R., “Has the time come for doing away with Cobalt-60 teletherapy for cancer treatments?” *Journal of Medical Physics*, 2009, 34(2): 63-65, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2805891/>.

¹³⁹ Page, Brandi R., Alana D. Hudson, Derek W. Brown, Adam C. Shulman, May Abdel-Wahab, Brandon J. Fisher, and Shilpen Patel, “Cobalt, Linac, or Other: What Is the Best Solution for Radiation Therapy in Developing Countries?” *International Journal of Radiation Oncology, Biology, Physics* 89(3): 476-480.

regulations. These rules address safe device use, including staff training, treatment planning, and dose administration. State regulatory agencies oversee linac use. Linac, gamma teletherapy, and SRS devices are subject to FDA certification requirements.

Disposal Costs and Considerations for Sealed Source Radiotherapy Devices

Due to a lack of commercial radioactive waste disposal options for high-activity sealed sources, the Federal Government has provided the only disposal option for gamma teletherapy and SRS devices. As a result, users do not pay the costs associated with device disposal, including transportation. The DOE NNSA Off-Site Source Recovery Program (OSRP) has recovered and disposed of 35 of these devices in the past decade.

Despite these challenges, the development of commercial disposal options for teletherapy and SRS sources is less problematic than it is for the cesium-137 sources used in most blood and research irradiators. Due to its relatively short half-life, even high-activity cobalt-60 sources such as disused teletherapy devices are now potentially disposable as Class B waste at existing commercial disposal facilities.¹⁴⁰ In some cases, cobalt-60 may be recovered from disused sources for recycling by a source manufacturer for use in cobalt-60 source applications that do not require high specific activities. As commercial disposal options become increasingly available for these and other high-activity sealed sources, these costs will be shifted back to device licensees, potentially adding tens or hundreds of thousands of dollars to the lifecycle costs that users must consider. According to publicly available information, the cost to dispose of a typical teletherapy or radiotherapy source at the only currently operational commercial disposal facility that allows nationwide access likely exceeds \$200,000.¹⁴¹ Furthermore, packaging and transportation of cobalt-60 sources above 0.4 TBq (10.8 Ci) require the use of specialized Type-B transportation containers, which could add tens of thousands of dollars more to the lifecycle cost of these devices.

¹⁴⁰ 2015 updates to NRC guidance clarifies that there are no activity limits on the classification of Co-60 sealed sources as Class B waste. The updated guidance has been approved for use by the low-level radioactive waste facility regulators for both U.S. Ecology in WA and WCS in Texas. U.S. Nuclear Regulatory Commission, “Branch Technical Position on Concentration Averaging and Encapsulation,” last updated October 26, 2016. <https://www.nrc.gov/waste/llw-disposal/llw-pa/llw-btp.html>.

¹⁴¹ Texas Administrative Code, Title 30, Part 1, Chapter 336, Texas Commission on Environmental Quality, Radioactive Substance Rules, Subchapter N, “Fees For Low-Level Radioactive Waste Disposal.”

Chapter 4: Alternative Technologies for Industrial Sterilization

Introduction

Industrial sterilization is primarily used for medical and healthcare products including: pharmaceuticals, cosmetics, and a wide range of single-use medical devices. These products account for approximately 80 percent of the industrial irradiation services produced in the United States on an annual basis.¹⁴² Common single-use medical devices include syringes, surgical gloves, masks, gowns, sutures, artificial joints and other implanted devices, medical tubing, and sterile solution containers. Most of the remaining 20 percent domestic industrial irradiation of capacity is used for materials and food-processing applications, including industrial polymer crosslinking, and the phytosanitary and pathogen reduction treatments addressed in Chapter 5 of this report.

The United States has the largest medical device market in the world at an estimated \$140 billion a year—equal to more than 40 percent of the global total.¹⁴³ There are more than 11,400 medical device companies employing more than 460,000 people in the country.¹⁴⁴ The total United States market for sterilization equipment and services is valued at approximately \$2 billion annually.¹⁴⁵ Medical device demand continues to grow at a 5 percent to 7 percent rate due to an aging population and greater global access to healthcare. As a result, worldwide demand for product sterilization is expected to increase at about the same rate. Between 35 percent and 40 percent of domestic United States medical device consumption is imported, and a similar share of domestic United States production is exported.¹⁴⁶ Foreign sales represent 40 percent to 50 percent of overall revenues for United States medical device companies when sales by foreign subsidiaries are taken into account.¹⁴⁷ Large medical product manufacturers operate their own sterilization facilities as well as utilizing third-party sterilization service providers. Smaller manufacturers—which comprise about 80 percent of the market—utilize third-party providers.

The choice of a sterilization method is an essential component of the sterile product development process. Primary sterilization method selection factors include the material composition of the product, its density, and its packaging configuration. However, nearly all disposable medical products manufactured in the United States are sterilized using either EtO or a radiation technology.¹⁴⁸ Depending on how the market is measured, EtO and cobalt-60 gamma irradiation each account for 40 percent to 50 percent of these sterilizations, with the remainder composed of e-beam and other methods including x-ray.¹⁴⁹ At present, the

¹⁴² Dethier, Philippe, Industrial & Sterilization Solutions (IBA), “Industrial Gamma and X-ray: ‘Same but Different,’” Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

¹⁴³ SelectUSA, “Medical Technology Spotlight,” U.S. Department of Commerce, accessed March 28, 2018, www.selectusa.gov/medical-technology-industry-united-states.

¹⁴⁴ Frost & Sullivan, “2012 Medical Devices Outlook: Setting the Stage for What’s Next,” April 28, 2016.

¹⁴⁵ Markets and Markets Research, “Sterilization Equipment Market: By Type, Product, End User & By Region – Forecast to 2021,” (September 2016).

¹⁴⁶ Medicare Payment Advisory Commission (MEDPAC), *Report to the Congress: Medicare and the Health Care Delivery System*, (Washington, DC: Medicare Payment Advisory Commission, June 2017) page 209.

¹⁴⁷ Ibid.

¹⁴⁸ Ethylene Oxide is abbreviated as EtO or EO. This paper uses the abbreviation EtO.

¹⁴⁹ Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (IIA), “A Comparison of Gamma, E-Beam, X-ray, and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products,” August 31, 2017, <http://iiaglobal.com/wp-content/uploads/2018/01/White-Paper-Comparison-Gamma-Eb-Xray-and-EO-for-Sterilisation.pdf>.

primary sterilization modality is EtO. Steam and dry heat processes are used primarily for reusable medical devices, a relatively small portion of the overall sterilization market.¹⁵⁰

Commercially Available Industrial Sterilization Technology—Isotopic and Alternatives

The FDA requires certain consumer products, including disposable medical devices, to be packaged and sterilized using an approved method and process before they are brought to market. The FDA generally requires a “sterility assurance level” (SAL) of 10^{-6} for invasive medical products—i.e., a one in a million probability of a live microbe or virus remaining on the product after processing. Non-invasive medical products—those intended only for contact with intact skin—are generally required to meet the lower sterility threshold of 10^{-3} SAL.

Regardless of the source or device type, ionizing radiation achieves sterilization in a broadly similar fashion. The radiation causes both direct and indirect damage in resident microorganisms and viruses. The direct effects arise from the ionization (removal of electrons) of biologically important molecules, including DNA. The indirect effects arise from the free radicals formed during the ionization of water molecules within the biological systems. These free radicals cause a variety of lethal or damaging effects in organisms. While the treatment technologies are very different, EtO also achieves sterilization through the chemical disruption of biologically important molecules, including DNA.¹⁵¹

Ethylene Oxide

Ethylene Oxide (EtO) has been in use for approximately 90 years and is currently used to sterilize about half of all medical products by volume. EtO sterilizes products through the highly potent chemical interaction of the EtO molecule with proteins and DNA in the contaminant microorganisms residing on the device. These chemical interactions disrupt and damage cell structures, ultimately resulting in the destruction of the microorganisms.¹⁵² EtO is used to process many products, some of which are incompatible with other sterilization techniques, including radiation processes. These materials may include polymers such as polyvinyl chloride (PVC), glass, polypropylene (PP), plastics thermoformed at low temperature, polyethylene terephthalate glycol (PETG), amorphous polyethylene terephthalate (APET), as well as some active pharmaceutical agents and biologics. In addition, EtO applications have expanded to include active pharmaceuticals, pharmaceutical packaging, pharmaceutical devices, and dental products, as well as some foods, food ingredients, and cosmetic materials.¹⁵³

EtO is used as a gas in EtO processing, although it is typically pressurized and stored as a liquid prior to use. The sterilization mechanism is DNA damage facilitated by moisture during the process.¹⁵⁴ EtO sterilization processing involves exposure within an air-tight and humidified chamber of the packaged product on pallets

¹⁵⁰ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version*, (Washington, DC: National Academies Press, 2008), 102-103.

¹⁵¹ Maxim Integrated, “Sterilization Methods and Their Impact on Medical Devices Containing Electronics,” Application Note 5068, <https://www.maximintegrated.com/en/app-notes/index.mvp/id/5068>.

¹⁵² Gisela C., C. Mendes, MD, Teresa R. S. Brandao, PhD, and Cristina L. M. Silva, PhD, “Ethylene oxide sterilization of medical devices: A review,” *Am J Infect Control*, November 2007, Vol. 35, I. 9, Pages 574–581.

¹⁵³ Nordion Inc. *Fiscal 2013 Annual Report*, page 15. See also, Federal Trade Commission vs. Steris Corporation, et al., *Opinion and Order*, United States District Court Northern District Of Ohio Eastern Division, Case No. 1:15 CV 1080, September 25, 2015.

¹⁵⁴ Lambert, Byron J., Todd A. Mendelson, and Michael D. Craven, “Radiation and Ethylene Oxide Terminal Sterilization Experiences with Drug Eluting Stent Products,” *AAPS PharmSciTech*, December 2011, Vol. 12, No. 4, DOI: 10.1208/s12249-011-9644-8.

of about three cubic meters. Depending on the size of the chamber, one to forty pallets may be processed in a load.¹⁵⁵

EtO-sterilized products must be packaged in a gas-permeable sterile barrier system to allow for the penetration and removal of EtO and other gases used in sterilization. Vacuum cycles drive humidity and EtO throughout the load. The sterile barrier packaging allows for the EtO necessary exposure while preserving the sterility of the product between sterilization and use. This type of packaging is typically more expensive than non-permeable sterile barrier packaging materials.¹⁵⁶

Effective EtO sterilization involves exposure of the packaged devices to a validated combination of humidity, EtO gas, temperature, and time within an airtight sterilization chamber.¹⁵⁷ These parameters can be tailored to suit particular products or materials while still adhering to industry process design guidance.¹⁵⁸ However, cycle times are relatively long, ranging from several hours to 1 or more days. In addition, since EtO is flammable and carcinogenic, a number of safety-related factors must be assessed when sterilizing with EtO. EtO emissions must also meet United States Environmental Protection Agency (EPA) standards. As a result of these rules and guidelines, the installation and maintenance of expensive safety and emissions control equipment and related worker training represent a significant cost for EtO facility start-up and operation.

Cobalt 60 Industrial Irradiators

Gamma irradiation has been in use by industry for more than 60 years. Worldwide, there are more than 200 gamma industrial irradiators utilizing approximately 440 megacuries (MCi)¹⁵⁹ of cobalt-60 to irradiate approximately 400 million cubic feet of product a year.¹⁶⁰ As of 2015, there were 51 gamma irradiators located at 44 sites within the United States.¹⁶¹ These facilities used an estimated 150 MCi of cobalt-60 to sterilize approximately 200 million cubic feet of product annually.¹⁶² Approximately 18 of those facilities use roughly 45 MCi to provide in-house services, while the remaining 30 use approximately 105 MCi to sterilize products on a contract basis.¹⁶³ Consistent with the industrial sterilization market more generally, approximately 80 percent of United States industrial gamma irradiation capacity is used to sterilize

¹⁵⁵ Lambert, Byron J., Todd A. Mendelson, and Michael D. Craven, "Radiation and Ethylene Oxide Terminal Sterilization Experiences with Drug Eluting Stent Products," *AAPS PharmSciTech*, December 2011, Vol. 12, No. 4, DOI: 10.1208/s12249-011-9644-8.

¹⁵⁶ Industrial & Sterilization Solutions (IBA), "Review of Radiation Sterilization Technologies for Medical Devices" (2013), page 12.

¹⁵⁷ Lambert, Byron J., Todd A. Mendelson, and Michael D. Craven, "Radiation and Ethylene Oxide Terminal Sterilization Experiences with Drug Eluting Stent Products," *AAPS PharmSciTech*, December 2011, Vol. 12, No. 4, DOI: 10.1208/s12249-011-9644-8.

¹⁵⁸ "Sterilization of health-care products—Ethylene oxide—Requirements for the development, validation and routine control of a sterilization process for medical devices," International organization for Standardization (ISO), 1st edition, May 1, 2007, <https://www.iso.org/obp/ui/#iso:std:iso:11135:ed-2:v1:en>. Related documents include ISO 10993-7:2008/Cor 1:2009 "Biological evaluation of medical devices Part 7: Ethylene oxide sterilization residuals," International Organization for Standardization, accessed March 22, 2019, <https://www.iso.org/standard/34213.html>.

¹⁵⁹ 1 million curies = 1 megacurie.

¹⁶⁰ Dethier, Philippe, Industrial & Sterilization Solutions (IBA), "Industrial Gamma and X-ray: 'Same but Different,'" Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

¹⁶¹ Gamma Industry Processing Alliance (GIPA), "Cobalt-60 Irradiation and Alternative Technologies," Presentation to the Alternative Technology Working Group (2015).

¹⁶² Dethier, Philippe, Industrial & Sterilization Solutions (IBA), "Industrial Gamma and X-ray: 'Same but Different,'" Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf; Gamma Industry Processing Alliance (GIPA), "Comparison of Cobalt-60 and X-Ray Technologies," GIPA Fact Sheet, 2007, http://gipalliance.net/wp-content/uploads/documents/GIPAFactsheet_XrayComparison_000.pdf.

¹⁶³ Gamma Industry Processing Alliance (GIPA), "Cobalt-60 Irradiation and Alternative Technologies," Presentation to the Alternative Technology Working Group (2015).

disposable medical products.¹⁶⁴ The remaining capacity is used for a variety of applications, including materials processing and to treat some food products, such as fruits, spices, and ground beef.¹⁶⁵

Industrial irradiation facilities include typical warehouse features, such as loading dock access, product conveyance mechanisms, and areas for temporary storage, as well as a shielded bunker where products are exposed to a radiation source. Product exposure typically involves conveyance of packaged products around a rack of cobalt-60 sources located in the center of the bunker. Products are placed in an irradiator container (also called a “cage” or “rack”) which make one or more passes around the source rack in order to obtain the prescribed dose. Most of these facilities use a wet storage configuration, whereby the cobalt-60 source rack is lowered into a shielded pool of water during breaks in product processing. Table 4.1 below provides additional detail on the primary features of a typical gamma irradiator processing facility: a biological shield, product handling system, radiation source, and safety and control systems.

The cobalt-60 source racks used in industrial irradiation facilities are typically comprised of 100 to a few thousand individual radiation sources. The welded, stainless steel sources are typically doubly encapsulated with an original activity ranging from 5,000 to 13,000 Ci. The 5.27-year half-life of cobalt-60 results in an approximate 12.3 percent loss in the source’s radioactivity each year. As a result, gamma facilities periodically adjust processing times to ensure that products receive the required dose.¹⁶⁶ In order to maintain a relatively constant throughput, these facilities typically add new sources to the source rack (the removal of existing sources may be required at the same time). Decayed sources are typically returned to the manufacturer after several half-lives.

Cobalt-60 emits gamma rays equally in all directions from the source until interacting with materials in their pathway. In order to process products as efficiently as possible, gamma irradiators are designed to optimize the amount of radiation absorbed by the target products, while at the same time achieving the required dose distribution in each package. Typically, about 30 percent of the energy emitted during industrial irradiation processing is usefully absorbed, although the amount varies from 15 percent to 40 percent, depending on the facility configuration and physical features of the packaged products. The remaining energy is absorbed into the structural material, pool water, or concrete walls.¹⁶⁷

The amount of energy deposited (absorbed dose) in a target material will vary through the depth of the material, independent of the radiation source and type. For the purposes of industrial irradiation, the dose will generally decrease as the radiation penetrates the packaged product. The dose distribution can be expressed in terms of DUR. Ratios closer to 1 indicate small variation in dose throughout the target, while ratios further from 1 indicate a greater difference between the highest and lowest dose areas within the irradiated product. For example, if a package or pallet is irradiated from two opposite sides simultaneously, the highest doses will generally be outside edges nearest the radiation source, with the lowest dose absorbed in the center. The actual DUR will vary depending upon the irradiation technology, the processing

¹⁶⁴ Gamma Industry Processing Alliance (GIPA), “Comparison of Cobalt-60 and X-Ray Technologies,” GIPA Fact Sheet; 2007, http://gipalliance.net/wp-content/uploads/documents/GIPAFactsheet_XrayComparison_000.pdf; International Atomic Energy Agency (IAEA), “Trends in Radiation Sterilization of Health Care Products,” (Vienna: IAEA, 2008), page 56.

¹⁶⁵ Gamma Industry Processing Alliance (GIPA), “Comparison of Cobalt-60 and X-Ray Technologies,” GIPA Fact Sheet; 2007, http://gipalliance.net/wp-content/uploads/documents/GIPAFactsheet_XrayComparison_000.pdf.

¹⁶⁶ Dethier, Philippe, Industrial & Sterilization Solutions (IBA), “Industrial Gamma and X-ray: ‘Same but Different,’” Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

¹⁶⁷ International Atomic Energy Agency (IAEA), “Trends in Radiation Sterilization of Health Care Products,” (Vienna: IAEA, 2008) page 11; Dethier, Philippe, Industrial & Sterilization Solutions (IBA), “Industrial Gamma and X-ray: ‘Same but Different,’” Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

configuration, and the physical characteristics of the packaged product. For industrial gamma irradiation, the DUR for a pallet irradiator is typically approximately 1.6 to 1.8 depending on the product¹⁶⁸ and 1.3 to 1.6 for a tote-type irradiator for medical products.

An important factor in determining the commercial potential for industrial sterilization is dwell time. For irradiation facilities, the dwell time of a target material in the radiation field depends on product density, required dose, facility configuration, and the cobalt-60 source activity. Packaged medical devices have a typical average density between 0.1 and 0.3 g/cm³.¹⁶⁹ The accepted standard to ensure sterility (a SAL of 10⁻⁶) is anywhere from 15,000 Gy to 35,000 Gy.¹⁷⁰ Selection of a particular sterilization dose depends on the expected bioburden of the product and is decided based on ISO 11137 and 13004.¹⁷¹

According to a recent assessment of medical device sterilization, a typical gamma irradiation facility is capable of an annual medical device throughput between 500,000 and 1.375 million cubic feet of product for every 1 MCi of cobalt-60 employed.¹⁷² This figure assumes a 25,000 Gy minimum dose across a range of product densities of 0.1 g/cm³ to 0.3g/cm.³ A facility using 4 MCi of cobalt-60 would therefore be capable of processing between 2 and 5.5 million cubic feet annually.¹⁷³

¹⁶⁸ Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (IIA), “A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products,” (November 2017).

¹⁶⁹ Dethier, Philippe, Industrial & Sterilization Solutions (IBA), “Industrial Gamma and X-ray: ‘Same but Different,’” Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

¹⁷⁰ 1 gray = 1000 kilogray.

¹⁷¹ ISO 11137 allows for other sterilization doses of 15 and 25 kGy. ISO 13004 includes 17.5, 20, 22.5, 27.5, 30, 32.5, and 35 kGy.

¹⁷² Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (iia), “A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products,” (November 2017).

¹⁷³ Ibid.

Table 4.1: Typical Cobalt-60 Industrial Irradiation Facility Features¹⁷⁴

BIOLOGICAL SHIELD	The biological shield is the structure that contains the source of radiation and provides attenuation of any radiation fields to levels that are safe for people working outside the shield area. The shield is most often constructed of concrete with an inner chamber containing the source and one or more interim sections through which product passes to enter the inner chamber. The shield may also be constructed of combinations of steel and/or lead in addition to or as an alternative to concrete as long as the resulting radiation fields outside the shield when the irradiator is operating fall within regulatory guidelines. When product is not being irradiated, the sources are stored in a deep-water pool, which also acts as a biological shield.
PRODUCT HANDLING SYSTEM	The product handling system is what transports the products into the irradiator, to the source, and then back out again. Product is loaded into or onto specially designed irradiation containers such as tote boxes, hanging carriers, or even pallets. The irradiation containers enter the shield through the interim section, pass into the inner chamber where they are indexed around the source, and then proceed back outside the shield where they are unloaded and readied for release. The radiation dose received by the product is a function of the design of the irradiator, the activity of the source, the density of the product, and the time spent in each position around the source.
RADIATION SOURCE	The source of radiation in most gamma irradiators is cobalt-60 in the form of double-encapsulated sealed sources. Multiple sources are arranged in a source rack, which is stored in a pool of water when not in use. The high-energy photons (gamma rays) emitted by cobalt-60 disrupt living cells by damaging DNA and other cellular structures. These photons induce changes at the molecular level, rendering organisms incapable of reproduction or causing their deaths. This enables the reduction of the microbial load on the product to the desired SAL.
CONTROL AND SAFETY SYSTEM	The control system of an irradiator is designed to provide both operational and safety functions. Multiple redundant safeguards are in place to ensure that the irradiator is not accessed during operation, as are operational health and safety controls around the product handling system. Modern irradiators are designed using a programmable logic controller platform. Faults and events are captured in a database and can be viewed on a computer screen for normal operation and troubleshooting.

¹⁷⁴ Adapted from Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (iia), "A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products," (November 2017).

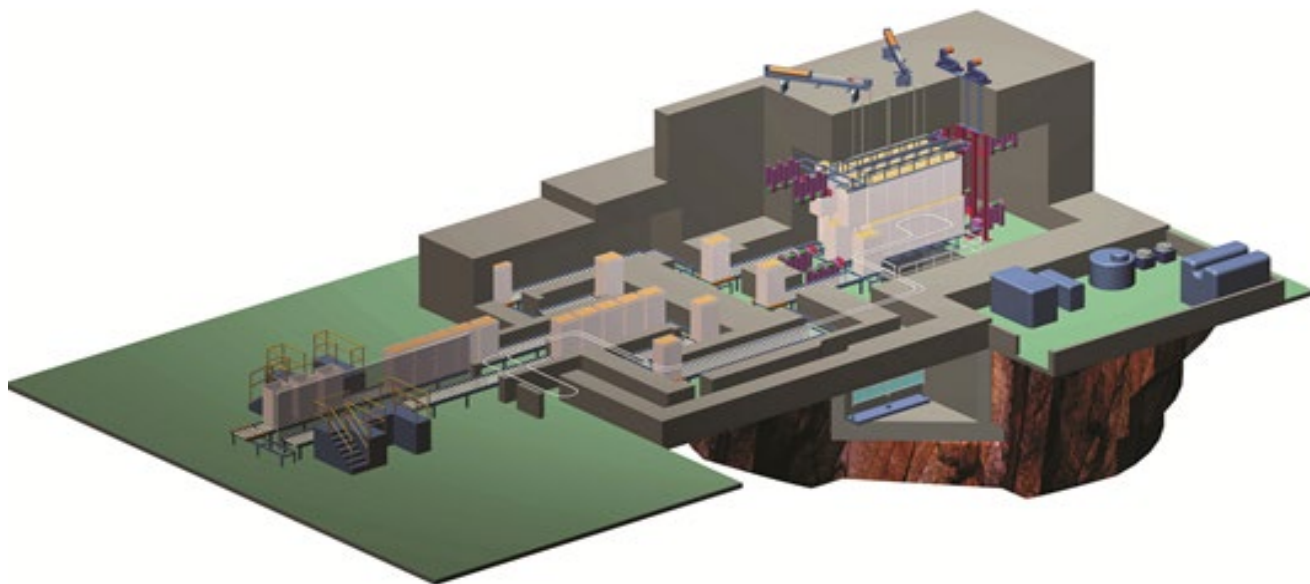


Figure 4: Typical Gamma Irradiator. (Diagram courtesy of Nordion (Canada) Inc)

Electron Beam Accelerators

The first facility to sterilize medical devices using the direct application of high-energy e-beam radiation began operations in 1956.¹⁷⁵ By the early 1990s, high-energy, high-power e-beam devices suitable for industrial scale processing had become available. The increased reliability of these devices made them cost-competitive with gamma and EtO for medical device sterilization.¹⁷⁶ Worldwide, less than 5 percent of disposable medical devices are currently sterilized using e-beam devices.¹⁷⁷ E-beam facilities have a similar layout to gamma processing centers, including loading dock access, areas for temporary storage, and a conveyance system to move products through a shielded irradiation bunker where the accelerator is located.

There are approximately 15 to 20 e-beam irradiation facilities in the United States, including at least 13 “in-house” e-beam facilities operated by large medical device manufacturers and two large multipurpose service centers, which charge customers for e-beam use by the hour or product load.¹⁷⁸ Several of the in-house facilities perform in-line sterilization processing, whereby irradiation takes place at the end of a continuous device production and packaging process.¹⁷⁹

Although accelerator technologies vary, all use electricity to generate and accelerate a beam of electrons at the target of interest. However, in contrast to the photon energy generated by both gamma sources and x-ray technologies, the electron energy produced by acceleration has a relatively short range and less ability to penetrate product. As a result, the density distribution and dose requirements within the packaged product

¹⁷⁵ Cleland, M. R., “Industrial applications of electron accelerators,” CAS 2005 - CERN Accelerator School: Small Accelerators, Proceedings. 10.5170/CERN-2006-012.383, (2006), <https://cds.cern.ch/record/1005393/files/p383.pdf>.

¹⁷⁶ International Atomic Energy Agency (IAEA), “Trends in Radiation Sterilization of Health Care Products,” (Vienna: IAEA, 2008) page 43.

¹⁷⁷ Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (IIA), “A Comparison of Gamma, E-Beam, X-ray, and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products,” August 31, 2017, <http://iiaglobal.com/wp-content/uploads/2018/01/White-Paper-Comparison-Gamma-Eb-Xray-and-EO-for-Sterilisation.pdf>.

¹⁷⁸ International Irradiation Association (IIA), “Industrial Radiation with Electron Beams and X-rays,” Rev. 6 (May 2011), page 82. Table XXII.

¹⁷⁹ International Irradiation Association (IIA), “Industrial Radiation with Electron Beams and X-rays,” Rev. 6 (May 2011).

are particularly important for industrial e-beam processing. To account for the limited penetration of the e-beam radiation, packaged products might be required to be customized to undergo e-beam sterilization. To achieve the required DURs, containers are often irradiated from two opposing sides, either using a processing mechanism that flips or rotates the target packages for a second exposure or employing two beam lines in opposite directions to irradiate both sides of the product without flipping or rotation.

E-beam penetration is primarily a function of the accelerator energy and the areal density of the target, a measure that takes into consideration both the size and weight of the packaged product.¹⁸⁰ Industrial e-beam accelerators range in energies from 1 MeV to 20 MeV, although 3 MeV to 10 MeV is typical for medical device sterilization.¹⁸¹ By one estimation, a 10 MeV accelerator may be used with areal densities up to 3.3 g/cm² (33 cm at 0.1 g/cc) if a single beam is used and up to 8.3 g/cm² (83 cm at 0.1 g/cc) when exposed from opposing sides.¹⁸² DURs for e-beam device applications are highly dependent on the homogeneity of the target product and beam energy; a typical range is approximately 1.3 to 1.5 on smaller box-sized targets¹⁸³, but DURs of greater than 2.0 are possible. Significant dose gradients can be present in non-homogeneous products. In addition, e-beam technologies are relatively energy efficient, converting approximately 10 percent to 50 percent of the electricity input into beam energy, depending on the accelerator technology and efficiency of the system.¹⁸⁴ However, the cost estimate is highly dependent on variables such as processing volumes and product density.

For products amenable to e-beam treatment, the application of the required dose is extremely rapid. Although dose rates will vary depending primarily on accelerator power, required doses are typically delivered to process containers in seconds.¹⁸⁵ Power levels typical for 3 MeV to 10 MeV industrial devices range from 15 kW to 800 kW;¹⁸⁶ these devices are capable of supplying tens of kilogray in seconds to the target.¹⁸⁷ The short exposure durations characteristic of e-beam irradiation may also help reduce the likelihood or extent of product discoloration or degradation relative to gamma processing.¹⁸⁸ However, the extremely short exposure time may not be as beneficial for killing aerobic organisms since the oxygen will not have a chance to replenish during the treatment. Some e-beam devices are capable of providing an adjustable range of electron energies and/or switching between e-beam and x-ray generation. As a result, the new generation of linacs has capabilities to customize energy and power for different applications.

In addition, compact superconducting radiofrequency (SRF) linac devices currently under development may provide additional benefits for medical device sterilization or other industrial irradiation applications, including lower overall system costs. SRF technologies provide continuous wave operation and high average

¹⁸⁰ Pillai, Suresh, "Principles of Ionizing Radiation and eBeam and X-ray Dose Deposition," Texas A&M E-Beam Workshop (2017).

¹⁸¹ Sugranes, Jorge, "Basic Operating Principles and Validation of Electron Beam Irradiation Systems," *Journal of Validation Technology*, November 2005; International Irradiation Association (IIA), "Industrial Radiation with Electron Beams and X-rays," Rev. 6 (May 2011).

¹⁸² Pillai, Suresh, "Principles of Ionizing Radiation and eBeam and X-ray Dose Deposition," Texas A&M E-Beam Workshop (2017).

¹⁸³ IOTRON, "The IOTRON Electron Beam Experience," Texas A&M E-Beam Workshop (2017).

¹⁸⁴ Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (IIA), "A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products" (2017).

¹⁸⁵ Lambert, Byron J., Todd A. Mendelson, and Michael D. Craven, "Radiation and Ethylene Oxide Terminal Sterilization Experiences with Drug Eluting Stent Products," *AAPS PharmSciTech*, December 2011, Vol. 12, No. 4, DOI: 10.1208/s12249-011-9644-8; Also Industrial & Sterilization Solutions (IBA), "Review of Radiation Sterilization Technologies for Medical Devices" (2013), page 11.

¹⁸⁶ While 800 kW is an upper limit, typically power of more than 100 kW is impractical for e-beam sterilization applications due to limitations on conveyor speeds.

¹⁸⁷ International Irradiation Association (IIA), "Industrial Radiation with Electron Beams and X-rays," Rev. 6 (May 2011), pages 82-85; Industrial & Sterilization Solutions (IBA), Practical Advantages of the Rhodotron, Whitepaper, <http://www.iba-industrial.com/downloads/sterilization-of-medical-devices/17>; Pillai, Suresh, "Principles of Ionizing Radiation and eBeam and X-ray Dose Deposition," Texas A&M E-Beam Workshop (2017).

¹⁸⁸ These effects result from the fast processing times associated with x-rays. See Philippe Dethier, Industrial & Sterilization Solutions (IBA), "Industrial Gamma and X-ray: Same but Different," Whitepaper, page 10, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf; E-beam processing is accomplished in seconds as opposed to minutes or hours for other technologies, reducing effects on sensitive materials. See Industrial & Sterilization Solutions (IBA), "Review of Radiation Sterilization Technologies for Medical Devices," (2013), page 11.

e-beam power with beam energies up to 10 MeV for sterilization (and higher for other applications).¹⁸⁹ SRF designs have already replaced conventional e-beam technologies in large-scale science accelerator projects. Like conventional linac technologies, compact SRF designs for sterilization applications could include adjustable energy output capabilities to facilitate uniform dose profiles across a wide range of product and package types, including low-density materials or surface-only sterilization. In addition, these devices can be designed to provide both e-beam and x-ray beam radiation.¹⁹⁰

Advanced non-superconducting linac devices are also under development. At least one accelerator manufacturer is developing 5 MeV to 10 MeV dual e-beam/x-ray systems capable of operating at significantly higher power than current designs.¹⁹¹ These advances are expected to result in increased processing capacity while maintaining or improving the DUR provided.

X-ray

X-rays were first used for industrial irradiation during the 1990s, however, they have not yet acquired a significant share of the industrial irradiation market. Currently, the United States, Europe, and Eastern Asia have the greatest number of high-power x-rays for industrial processing and research applications, although few are used to sterilize medical devices.¹⁹² There are currently two commercial contract sterilization facilities, one in California¹⁹³ and a larger facility in Switzerland.¹⁹⁴

Industrial x-ray irradiation facilities, like gamma and e-beam processing centers, include transportation access and storage areas, product conveyance and handling systems, and a shielded bunker housing the radiation source, in this case one or more x-ray devices. The conveyance and handling systems pass packaged products through one or more x-ray beams to achieve the required dose.

¹⁸⁹ Superconducting linacs efficiently convert radiofrequency power to beam power and, because the operation takes place in helium bath and thus solves heat transfer problems at the cavity surface, can operate continuously. The features of turnkey electron linacs include a helium cryoplant, microwave power, and an electron source. New designs for superconducting linacs are emerging that reduce the necessity of handling cryogenic liquid helium, which will further advance their turnkey capability.

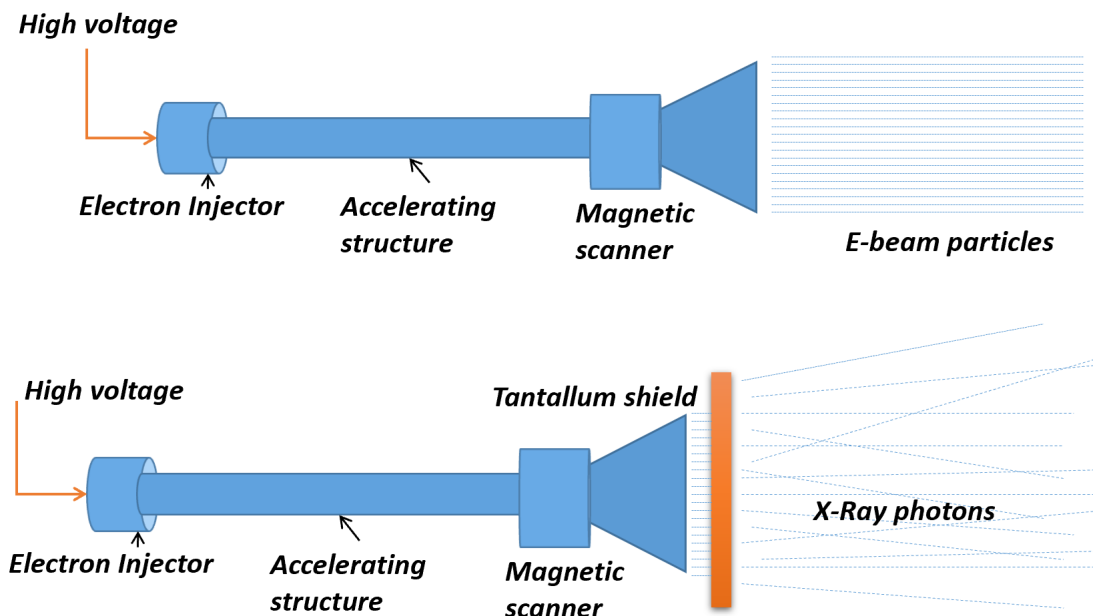
¹⁹⁰ Kroc, Thomas K., Jayakar C. T. Thangaraj, Richard T. Penning, and Robert D. Kephart, "Accelerator-Driven Medical Sterilization to Replace Co-60 Sources," Fermi National Accelerator Laboratory, July 6, 2017.

¹⁹¹ Presentation of Philippe Dethier, MEVEX, "Megawatt Sterilization Systems," presentation to the April 2019 International Meeting on Radiation Processing (IMRP) in Strasbourg, France.

¹⁹² International Irradiation Association (IIA), "Industrial Radiation with Electron Beams and X-rays," Rev. 6 (May 2011).

¹⁹³ *Federal Trade Commission v. Steris Corporation*, No. 1:15 CV 1080, 2015 WL 5657294, (N.D. Ohio, September 24, 2015).

¹⁹⁴ Steri-Tek, website, 2018, <https://steri-tek.com/>.



X-rays generated for industrial applications are typically produced using a 5 MeV to 7.5 MeV¹⁹⁵ e-beam accelerator with at least 80 kW of power to strike a tungsten or tantalum target with a high energy beam of electrons.¹⁹⁶ The collision of the accelerated electrons with the heavy-metal target produces x-rays (bremsstrahlung radiation). This radiation impacts targeted products in a similar manner as the gamma rays from cobalt-60. However, while cobalt-60 gamma rays are produced at specific and discrete energies, the produced x-rays are comprised of a broad spectrum of energies, ranging as high as the electron accelerator that produced them.

The x-rays generated using 5 MeV to 7.5 MeV electron accelerators, having a spectrum of energies with an average of about 1.67 MeV to 3.33 MeV respectively, can penetrate products somewhat more effectively than both cobalt-60 (1.25 MeV avg) and e-beam technologies. In typical processing pallet size product volumes, x-rays can provide DUR under 1.3.¹⁹⁷ Most high-powered x-rays devices have an adjustable energy output level, enabling relatively uniform dose profiles, even in thick, high-density targets.¹⁹⁸ These features may enable x-ray processing of devices previously only amenable to EtO treatments.¹⁹⁹

¹⁹⁵ X-rays may be produced as high as 10 MeV, but are typically limited to 7.5 MeV to avoid photo-activation.

¹⁹⁶ Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (iia), "A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products," (2017).

¹⁹⁷ IBA, "Review of Radiation Sterilization Technologies for Medical Devices," Whitepaper, 2013, <http://www.iba-industrial.com/downloads/sterilization-of-medical-devices/17>, noting that "[a]ctual dosimetry results have demonstrated that full pallet loads of dimensions 100 x 120 x 180 cm with a homogeneous density of 0.15 g/cm³ achieve dose uniformity ratio of 1.25.

¹⁹⁸ International Irradiation Association (IIA), "Industrial Radiation with Electron Beams and X-rays," Rev. 6 (May 2011).

¹⁹⁹ Galloway, Rick, Industrial & Sterilization Solutions (IBA), "X-ray: The emerging alternative to gamma irradiation," Texas A&M University Hands-On Workshop in E-Beam Irradiation Technologies, (2017).

According to one accelerator manufacturer, the additional cost to add x-ray capabilities to a 5 MeV to 7.5 MeV e-beam facility at the time of construction is approximately 10 to 15 percent, including conveyor upgrades and additional shielding.²⁰⁰ Facilities utilizing such dual technology systems may be able to process a wider range of products than single-technology locations. In addition, these systems could reduce the cost and uncertainties for some medical device providers to transition from e-beam to x-ray when beneficial. At least two of the 15 - 20 e-beam service locations in the United States also have x-ray irradiation capabilities.²⁰¹

Industrial x-rays can deliver the high doses required for device sterilization very rapidly, supplying hundreds to thousands of Gy per minute.²⁰² In addition to enabling reduced processing times, high dose rates may also help reduce the negative effects, such as odor generation, material instability, and color change, that irradiation can have on sensitive products.

Relative to gamma rays, x-rays are unidirectional, resulting in a greater percentage of the energy generated hitting the target.²⁰³ However, a primary disadvantage of x-ray irradiation is the loss of energy that takes place during the bremsstrahlung creation process, primarily as the result of heat generation. Only 5 to 13 percent of the e-beam energy is converted into x-rays, with conversion efficiency directly correlated to accelerator energy. Typical conversion efficiencies are approximately 8 percent for 5 MeV, 12 percent for 7 MeV, and 13 percent for 7.5 MeV.²⁰⁴

Technology Purchase and Replacement Considerations

Accelerator design improvements have increased the potential for both e-beam and x-ray to replace gamma for industrial applications. However, the selection by medical device manufacturers of a sterilization method typically also depends on complex business and regulatory factors. The discussion here attempts to identify the various technical, business, and regulatory factors and provide a spectrum of industry perspectives on how they may impact user (and irradiation service provider) choices.

E-beam proponents note the ability to design in-line e-beam irradiation systems and the improving cost efficiency of e-beam as key drivers for machine sources to replace gamma irradiation.²⁰⁵ Whether x-ray technology will capture significant market share from gamma or e-beam technologies for medical device sterilization will depend on a number of factors, most important of which is the product volume available for sterilization. That is, until there is clearly sufficient demand for x-ray sterilization services, it seems unlikely that sterilization service providers will invest in x-ray facilities and that x-ray will capture a meaningful portion of the market.

For example, the ability of x-ray irradiation to more quickly process pallet-sized target volumes than gamma sources may provide significant competitive advantages for x-ray over both gamma and e-beam technologies. Its proponents expect that, in the long term, “many dedicated x-ray sterilization centers will be built, progressively taking over sterilization of new and existing products.”²⁰⁶ According to these

²⁰⁰ Massaro, Gino, E-beam and X-ray Technologies: innovative solutions, IBA Presentation, March 5, 2015, [http://iiaglobal.com/uploads/documents/S2.35%20Massaro%20\(IBA\)%20.pptx](http://iiaglobal.com/uploads/documents/S2.35%20Massaro%20(IBA)%20.pptx)

²⁰¹ International Irradiation Association (IIA), “Industrial Radiation with Electron Beams and X-rays,” Rev. 6 (May 2011).

²⁰² Pillai, Suresh, “Principles of Ionizing Radiation and eBeam and X-ray Dose Deposition,” Texas A&M E-Beam Workshop, (2017).

²⁰³ FNAL input.

²⁰⁴ International Irradiation Association (IIA), “Industrial Radiation with Electron Beams and X-rays,” Rev. 6 (May 2011).

²⁰⁵ Subject matter input to the Working Group, August 2018.

²⁰⁶ Industrial & Sterilization Solutions (IBA), “Ahead of the curve,” IBA Whitepaper, 2014, page 1, www.iba-industrial.com/downloads/sterilization-of-medical-devices/17.

assessments, service contractors are likely to be the first to adopt the new technology, followed by large manufacturers operating in-house medical device sterilization operation for their own products.²⁰⁷ But this process may require new conveyor designs to optimize throughput.

However, other industry participants believe that the faster and more energy-efficient processing enabled by e-beam irradiation for many products compensates for the additional product handling required to process small volumes. Furthermore, the cost of transporting finished products to third-party sterilization centers is increasing, and some major medical device companies are considering bringing sterilization technologies in-house. In this scenario, the use of custom-designed in-line e-beam sterilization systems may become attractive.

A non-proprietary capital comparison of e-beam and x-ray facilities was not available at the time of the writing of this white paper.

Processing Costs

Improved accelerator technologies have made new e-beam and x-ray sterilization processing more cost-effective. However, actual processing costs are highly dependent on situational factors, such as processing volume, facility proximity, and other logistical constraints.

For example, one large, multinational medical device manufacturer, utilizes both in-house and contract sterilization services for its products, including gamma, e-beam, and EtO processing. It identifies similar processing volume and costs for gamma and EtO overall, although these costs vary significantly among processing locations, depending on the volume processed. Although the company only uses e-beam sterilization on a proportionally limited basis—for roughly a third of the volume as each of the other two technologies—it estimates that its e-beam processing costs per volume are roughly half of those for gamma and EtO. The company does not use x-ray sterilization for its products.

Gamma and X-Ray Comparative Assessments

More general irradiation technology cost comparisons are very difficult to make for medical device sterilization because of the large number of variables, as well as the measurement challenges inherent in comparing input values measured in Ci with those measured in watts of electricity. In addition, the primary variable costs of the different radiation technologies, including electricity for e-beam and x-ray and radioactive source replenishment for cobalt-60 irradiation, may vary significantly over time and by location.²⁰⁸ However, several simplified assessments have been undertaken by industry organizations comparing gamma and x-ray sterilization.²⁰⁹ While the studies use different methods and arrive at different conclusions, they are nevertheless helpful for identifying the key cost-consideration factors.

²⁰⁷ Industrial & Sterilization Solutions (IBA), “Ahead of the curve,” IBA Whitepaper, 2014, page 1, www.iba-industrial.com/downloads/sterilization-of-medical-devices/17.

²⁰⁸ For example, industry sources indicate that the curie cost of Co-60 has increased significantly in recent years. However, supplier prices are not publicly available.

²⁰⁹ Dethier, Philippe, Industrial & Sterilization Solutions (IBA), “Industrial Gamma and X-ray: ‘Same but Different,’” Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf; Sugden, S., “Relative Economics and Practicalities of Gamma and X-ray Sterilization”, Panel on Gamma and Electron Irradiation, 2016 Gamma Industry Processing Alliance (GIPA), “Comparison of Cobalt-60 and X-Ray Technologies,” GIPA Fact Sheet, 2014.

An analysis by IBA, a large accelerator manufacturer, compares the cost-efficiency of gamma and x-ray processing across a five-year timeframe.²¹⁰ IBA uses product density and throughput assumptions for application of a 25,000 Gy dose. For a 7 MeV x-ray, these result in a power conversion ratio of 1 MCi to 124 kW for cost-comparison purposes.²¹¹ For the cost comparison, IBA uses range-estimates for the cost of electricity and cobalt-60 source replenishment, including transportation. In addition, the assessment amortizes the initial cost of the x-ray device over the five-year timeframe and an annual maintenance charge is added.²¹² This results in worst-case, average-case, and best-case scenarios for both technologies.

As depicted in Figure 4.4,²¹³ the IBA assessment concluded that the amortized capital cost of an x-ray system requires a minimum processing volume in order to be cost-effective. Even under the worst-case scenario for gamma systems and best-case scenario for x-ray, cobalt-60 processing will be more cost-effective, irrespective of cost assumptions, than x-ray for capacities requiring approximately 0.9 MCi or less. Further capacity increases are less expensive for x-ray than for gamma. As a result, even under the best-case scenario for gamma systems and the worst-case scenario for x-ray, x-ray systems should be more cost-effective than gamma systems for capacities requiring approximately at least 2.3 MCi of cobalt-60.²¹⁴ The remaining combinations of best, average, and worst-case scenario for the two technologies fall in between these two outcomes.²¹⁵

²¹⁰ Dethier, Philippe, Industrial & Sterilization Solutions (IBA), "Industrial Gamma and X-ray: 'Same but Different,'" Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

²¹¹ IBA estimates that yearly electrical cost for their accelerators is between USD 210,000 and 450,000 per MCi equivalence.

²¹² Philippe Dethier, Industrial & Sterilization Solutions (IBA), "Industrial Gamma and X-ray: 'Same but Different,'" Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

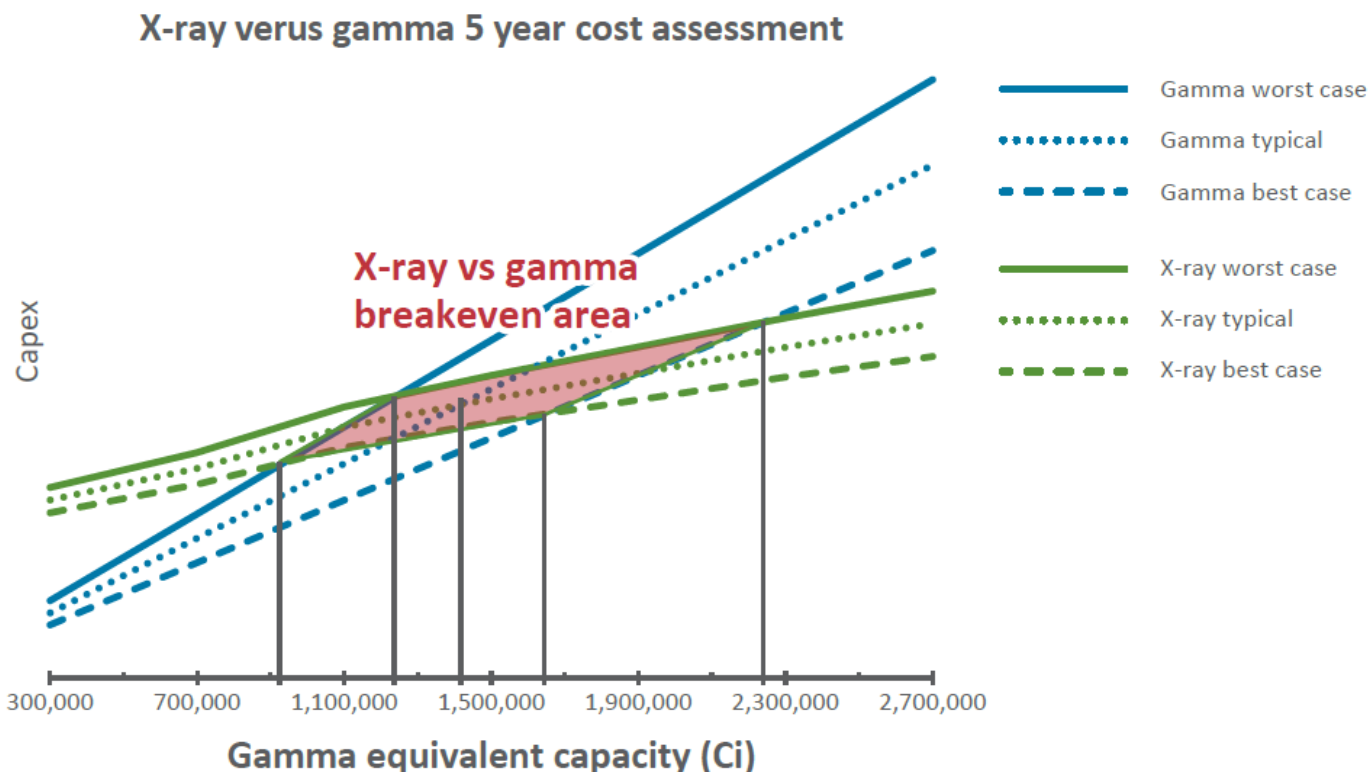
²¹³ The point of intersection in this figure has been challenged within the radiation industry and is subject to some uncertainty.

²¹⁴ Galloway, Rick, Industrial & Sterilization Solutions (IBA), "X-ray: The emerging alternative to gamma irradiation," Texas A&M University Hands-On Workshop in E-Beam Irradiation Technologies, (2017).

²¹⁵ Under a worst-case scenario for both gamma and x-ray, Co-60 gamma processing will be more cost effective than x-ray for capacities requiring up to 1.2 MCi of Co-60 or less. Under average-case assumptions for both gamma systems and x-ray, x-ray processing is more cost-effective than gamma in facilities with a capacity requiring greater than 1.4 MCi of Co-60. Under best case scenarios for both gamma and x-ray scenario, Co-60 processing will be more cost-effective than x-ray for capacities requiring up to 1.7 MCi of Co-60.

Figure 4.4²¹⁶

X-ray versus gamma



The results of a 2014 analysis by the Gamma Industry Processing Alliance (GIPA) are different.²¹⁷ The GIPA analysis estimates x-ray and gamma costs for processing equal volumes at 25,000 Gy. However, the GIPA paper provides a streamlined analysis, focusing on electricity and cobalt-60 costs during a single-year timeframe. To determine kW to Ci equivalence for a cost comparison, the GIPA analysis adapts throughput data published for several industrial and x-ray and gamma irradiation product densities and processing configurations.²¹⁸ The assessment normalizes the data to reflect gamma processing with just 1 MCi of cobalt-60. For x-ray processing, the GIPA analysis estimates the conversion of e-beam power to x-ray at 8 percent for a 5 MeV accelerator, with an increase photon yield of 60 percent for a 7.5 MeV accelerator, or about a 12.8 percent conversion efficiency.

Based on these assumptions, a power conversion ratio of 1 MCi to about 90-140 kW is calculated for a 7.5 MeV x-ray device. For x-ray costs, the GIPA assessment uses a kilowatt per hour range-estimate. For the cost

²¹⁶ The color scheme for this figure was modified for readability when placed in this chapter.

²¹⁷ Gamma Industry Processing Alliance (GIPA), "Comparison of Cobalt-60 Gamma and X-Ray Technologies," GIPA Fact Sheet, 2014.

²¹⁸ See footnotes 1 and 2 of the GIPA analysis, Gamma Industry Processing Alliance (GIPA), "Comparison of Cobalt-60 Gamma and X-Ray Technologies," GIPA Fact Sheet, 2014.

of gamma processing, annual replenishment of decayed cobalt-60 at \$2 per Ci is assumed. The resulting cost comparison from the GIPA analysis is shown in Table 4.2: 2014 GIPA Analysis: X-Ray and Gamma Cost Comparison below.

Table 4.2: 2014 GIPA Analysis: X-Ray and Gamma Cost Comparison

X-Ray (1 MCi equivalent)		Gamma/Cobalt-60 (1 MCi)
Electricity Cost (US\$/kW-h)	Power Utilization Cost 5 MeV 7.5 MeV	12.3% decay per year 123,244 Ci/y decay \$2.00 US\$/Ci ~\$250,000 per year
0.09	\$1,365,000 \$540,000	
0.10	\$1,515,000 \$600,000	
0.11	\$1,670,000 \$660,000	
0.12	\$1,820,000 \$720,000	

GIPA concludes that “the power utilization of Cobalt-60 is higher than that of x-ray irradiator technology, which in turn leads to lower operational costs for a commercial Cobalt-60 gamma irradiator than has been observed for x-ray irradiators.”²¹⁹

Table 4.3: IBA and GIPA X-Ray and Gamma Processing: Assumptions in Comparison compares the assumptions used in the IBA and GIPA assessments:

Table 4.3: IBA and GIPA X-Ray and Gamma Processing: Assumptions in Comparison

Assumption	IBA	GIPA
Product density (g/cm ³)	0.15	0.1 to 0.3
Dose (kGy)	25	25
X-ray accelerator energy	7 MeV	5 MeV – 7.5 MeV
X-ray conversion efficiency	Included but unspecified*	8% to ~12.8%
MCi/kW equivalence	1 MCi = 124 kW	1 MCi = 140kW to 90 kW
Throughput rate per MCi (m ³ /hour)	3.44	2.2 – 4.0
X-ray electricity cost (\$/kW hour) ²²⁰	\$0.05 to \$0.09	\$0.09 to \$0.12
X-ray capital costs	Included but unspecified*	n/a
X-ray maintenance costs	Included but unspecified*	n/a
Cobalt-60 replenishment cost (\$/ Ci)	\$2.50 – \$3.00	\$2.00
Cobalt-60 replenishment transport costs/fees (\$/year)	\$25,000 – \$50,000	n/a
Cobalt-60 disposal/decommissioning (\$/Ci)	\$0 to \$0.10	n/a
*IBA states that its analysis included this factor but does not indicate what value was assigned to the variable.		

²¹⁹ Gamma Industry Processing Alliance, (GIPA) “Comparison of Cobalt-60 Gamma and X-Ray Technologies,” GIPA Fact Sheet, 2014.

²²⁰ Electricity costs will vary based on locality and can range from \$0.05–\$0.40.

Cobalt-60 Supply and Price Constraints

Industrial sterilization facilities depend on a steady supply of encapsulated cobalt-60 to regularly replace decayed sources. However, the worldwide supply of cobalt-60 is subject to current and potential supply constraints that may impact the operational cost of panoramic irradiation relative to alternatives.²²¹

There are currently two types of operational power reactor commonly used to produce cobalt-60. The first is a Canadian design, known as a CANDU reactor, and the other is a Russian design known as the RBMK. There are 18 CANDU reactors located in Ontario, Canada, of which only 7 are currently producing cobalt-60. Additionally, there are CANDU reactors in China, Argentina, Romania, South Korea and India, some of which currently produce cobalt-60. There are 11 RBMK reactors in Russia, only 7 of which are currently producing cobalt-60. Cobalt-60 is also produced in research reactors such as the 3 reactors at Mayak and Dmitrovgrad Russia. The typical irradiation time to produce cobalt-60 is about 18 months to three years in CANDU reactors and up to five years in the RBMK reactors.²²²

However, in the next 5 to 10 years, a significant number of these reactors are scheduled to cease operations or undergo maintenance outages. In Canada, the Ontario Power Generation (OPG) reactors, are scheduled to permanently cease operations in 2024.²²³ In addition, the other four cobalt-60 production reactors in Canada are scheduled for a refurbishment process that will extend their lives, and cobalt production capability until 2064. During the refurbishment, one reactor at a time will be taken off-line, reducing the amount of cobalt produced during this 10-year period. During the next 15 years Russia will phase out its RBMK reactors and replace them with newer “VVER” designs which have the potential to produce cobalt-60.²²⁴

Nordion (Canada) Inc., the industry’s largest cobalt-60 supplier, among others, is taking steps to increase the global supply of cobalt-60 by:

1. Extending contracts with reactors currently producing cobalt
2. Working with the owners of the other CANDU reactors currently not producing cobalt
3. Bringing more RBMK reactors into cobalt-60 production
4. Acquiring and deploying technology to produce cobalt in light water reactors (of which there are more than 90 operational in the United States and more than 350 globally). In February 2019, the company stated that the “technology's viability has already been demonstrated in a pilot program that successfully produced approximately one million Curies [sic] of Cobalt-60 at two United States reactors.”²²⁵ The company has not yet provided a timeline or supply estimates for expanded production using the new technology

²²¹ Working Group member comments. See also, *Federal Trade Commission vs. Steris Corporation, et al.*, Plaintiff Federal Trade Commission's Complaint for Temporary Restraining Order and Preliminary Injunction, United States District Court Northern District Of Ohio Eastern Division, Case No. 1:15 CV 1080, June 4, 2015, page 5: “Some customers are concerned about the availability and pricing of gamma sterilization in the future due to questions about the supply of Cobalt 60. As a result, e-beam may become a closer economic substitute for gamma than it is today.”

²²² World Nuclear Association, “Radioisotopes in Medicine,” accessed January 2019, <http://www.world-nuclear.org/information-library/non-power-nuclear-applications/radioisotopes-research/radioisotopes-in-medicine.aspx>.

²²³ Ontario Energy Board, Province of Ontario, Canada, “Ontario’s Long Term Energy Plan 2017: Delivering Fairness and Choice,” <https://www.ontario.ca/document/2017-long-term-energy-plan>.

²²⁴ World Nuclear Association, “Radioisotopes in Medicine,” accessed January 2019, <http://www.world-nuclear.org/information-library/non-power-nuclear-applications/radioisotopes-research/radioisotopes-in-medicine.aspx>.

²²⁵ Sotera Health, “Nordion Acquires Technology to Expand Future Global Cobalt-60 Supply” <https://www.nordion.com/nordion-acquires-technology-to-expand-future-global-cobalt-60-supply/>

Maintenance, Reliability, and Downtime

Planned maintenance requirements for gamma source and accelerator-based sources differ in type and frequency, although the resulting facility downtimes may be similar. E-beam and x-ray facilities usually schedule between 30 and 50 hours per year of preventive maintenance, while gamma facilities typically undertake cobalt-60 source replenishment operations on an annual basis, a process that requires one or more days of downtime to complete.²²⁶ Gamma irradiation operations also require a limited amount of scheduled downtime to accommodate source-related maintenance and regulatory inspection activities.²²⁷

Most unplanned service interruptions at industrial irradiation facilities are the result of problems with facility features that gamma systems and accelerator-based sources have in common, such as product conveyance systems and process control software. E-beam and x-ray facilities must deal with downtimes arising from machine or subsystem malfunctions. Gamma, x-ray, and e-beam facilities have similar planned and unplanned maintenance costs related to these common features.²²⁸ However, contrary to gamma facilities, e-beam and x-ray facilities require staff capable of diagnosing and fixing accelerator malfunctions. Depending on site experience, the device manufacturer may have to send staff to sites for more complex issues. The number of qualified and trained professionals who have demonstrated experience operating, troubleshooting, and repairing e-beam and x-ray systems in the United States and elsewhere is currently in short supply. However, as e-beam and x-ray installations increase, it is expected that training programs for operators and repair personnel will become available to increase the pool of qualified personnel.

Industry representatives appear to disagree, however, regarding the unplanned downtime typical for accelerator-based industrial irradiation technologies. For example, one accelerator manufacturer recently cited availability rates above 97 percent for both x-ray and e-beam facilities, noting that, like gamma, these radiation sources rely on few moving parts, making them generally reliable, particularly relative to the mechanical conveyance and infrastructure systems common to all three system types.²²⁹ By contrast, a recent gamma industry assessment states that, while industrial accelerator systems have achieved “greater than 80 percent reliability in limited operations, some experience in the industry has shown that the uptime may be less than 75 percent for designs that convert to x-ray.”²³⁰ It is not surprising that there is significant variability in the reported downtime of e-beam equipment, as there is considerable variability in the quality of the e-beam systems that are commercially available today. Downtimes of e-beam and x-ray equipment will show country-by-country variation.

Regulatory Costs and Considerations

FDA Clearance and Sterilization

The FDA requires virtually all new medical devices to meet certain requirements before they can be sold or marketed in the United States. Sterile medical devices must be approved through the FDA’s Pre-Market Approval (PMA) process or be cleared through its 510(k) Premarket Notification program as “substantially

²²⁶ Philippe Dethier, Industrial & Sterilization Solutions (IBA), “Industrial Gamma and X-ray: ‘Same but Different,’” Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

²²⁷ Ibid.

²²⁸ Ibid.

²²⁹ Ibid.

²³⁰ Gamma Industry Processing Alliance (GIPA), “Comparison of Cobalt-60 Gamma and X-Ray Technologies,” GIPA Fact Sheet, page 3, 2014.

equivalent” to a previously cleared “predicate” device.²³¹ Although a demonstration of substantial equivalence to a predicate device requires submission of substantial product design and intended use information, the 510(k) clearance process enables manufacturers of most devices to forgo the much more expensive and time-consuming testing and validation required for a PMA. In 2015, for example, the FDA cleared more than 3,000 devices through the 510(k) program, while only 47 devices underwent the entire PMA process.²³²

For devices labeled as sterile, 510(k) clearance requires manufacturers to provide information that indicates that the sterilization method and process used for the device results in the necessary SAL. The FDA recognizes ionizing radiation, EtO, and heat as established sterilization methods for which consensus international standards are available.²³³ The FDA requires medical device manufacturers using these methods and standards to submit less extensive sterilization validation information than is required when methods without consensus standards or novel methods are used.²³⁴

However, even when radiation, EtO, or heat is used, the 510(k) application must include a description of the method used by the manufacturer to validate that the packaging configuration, loading pattern, and treatment process consistently result in the required SAL.²³⁵ For radiation sterilization this includes the method used to confirm that the selected radiation dose is adequate to reliably achieve product sterility while not adversely impacting device functionality.²³⁶

The time and cost for manufacturers to develop this information varies widely due to differences in technology and product. It would include testing for functionality, packaging, and biocompatibility and might include product sterility, method suitability, accelerated aging, and verification dose. Products that are marketed internationally can require the regulatory approval of multiple countries and agencies. While the use of international standards has made some of these approvals easier, requirements often still vary by product and nation.

²³¹ U.S. Food and Drug Administration (FDA), “The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]: Guidance for Industry and Food and Drug Administration Staff,” July 28, 2014, www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM284443.pdf.

²³² Hayes, Inc., “510(k) vs. PMA: Do you know the difference?” Hayes Evidence Blog, December 21, 2016, <http://blog.hayesinc.com/blog-what-is-the-510k-exemption-process-for-devices>.

²³³ ANSI/AAMI/ISO 11137-1:2006/(R)2010, Sterilization of Health Care Products - Radiation - Part 1: Requirements for Development, Validation, and Routine Control of a Sterilization Process for Medical Devices [Including: Amendment 1 (2013)], ANSI/AAMI/ISO 11137-2:2013, Sterilization of Health Care Products - Radiation - Part 2: Establishing the Sterilization Dose, and ANSI/AAMI/ISO 11137-3:2006/(R)2010, Sterilization of Health Care Products - Radiation - Part 3: Guidance on Dosimetric Aspects. ANSI/AAMI/ISO 11135:2014, Sterilization of Health Care Products - Ethylene oxide - Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices and ANSI/AAMI/ISO 10993-7 Biological Evaluation of Medical Devices, Part 7: Ethylene Oxide Sterilization Residuals. ANSI/AAMI/ISO 20857:2010, Sterilization Of Health Care Products - Dry Heat - Requirements for the Development, Validation and Routine Control of a Sterilization Process for Medical Devices and ANSI/AAMI/ISO 17665-1:2006/(R)2013, Sterilization of Health Care Products - Moist Heat - Part 1: Requirements for the Development, Validation, and Control of a Sterilization Process for Medical Devices.

²³⁴ The FDA also recognizes several additional sterilization methods, used primarily in specialized applications, as established even though no consensus standards exist (e.g., hydrogen peroxide and ozone [O₃]). Sterilization methods not identified as established are considered “novel” and must be supported by more robust testing information as part of the 510(k) process. See, U.S. Food and Drug Administration (FDA), “Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile Guidance for Industry and Food and Drug Administration Staff,” issued on January 21, 2016.

²³⁵ U.S. Food and Drug Administration (FDA), “Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile: Guidance for Industry and Food and Drug Administration Staff,” issued on January 21, 2016. The FDA-recognized sterile packaging standards include ISO 11607-1:2006 Packaging for Terminally Sterilized Medical Devices -- Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems and ISO 11607-2:2006 Packaging For Terminally Sterilized Medical Devices -- Part 2: Validation Requirements for Forming, Sealing and Assembly Processes.

²³⁶ ANSI/AAMI/ISO TIR13004:2013, Sterilization of health care products — Radiation —Substantiation of a Selected Sterilization Dose.

It is not possible to say that gamma, e-beam, x-ray, or EtO is preferable under any or all conditions—or even that one modality will always be preferred under the same conditions in different locations. Even among the three radiation technologies, the best option for a given location is a site-specific consideration that must take into account the available infrastructure, including space, utilities, and transportation access; the physical and technical resources available, such as skilled labor and repair capability; the type and volumes of products to be sterilized; and the relative costs associated with these factors.

Technology considerations for medical device manufacturers bringing a new device to market:

- **Product construction, density, geometry, materials, and heterogeneity**, which will help to determine the ability of a sterilization modality to penetrate the packaging and sterilize the product without degrading the materials used in either. Among irradiation technologies additional variables include the dose and dose uniformity requirements, and repeatability of dose delivery.²³⁷
- **Predicate device validation** because the vast majority of new devices rely on predicate devices for FDA clearance through the 510(k) process. To maintain the link between the old and new product, the sterilization modality needs to be the same.
- **Sterilization process validation** for materials to be sterilized and to obtain necessary approvals to utilize the irradiation technology for sterilization of each specific product.
- **Stricter regulations on EtO residues on products.**
- **Potential shortages and cost hikes for isotope and commercial sterilization costs.**

Technology considerations for sterilization service providers:

- **Sterilization timeline requirements** to determine irradiator size and its capability to meet effective, efficacious and reliable sterilization demands on an ongoing basis. Furthermore, timeline requirements could determine whether one or multiple irradiators are required to meet sterilization demand.
- **Product volume** to determine size and irradiator capacity needed now and in the foreseeable future.
- **Capital cost** such as initial and ongoing capital costs for irradiator and associated equipment, as well as considerations about whether one or more units will be required to deal with product volume and timeline.
- **Maintenance and service repair downtime and costs** such as expected irradiator reliability, irradiator equipment and source complexity, spare parts availability and cost, availability of timely service and repair, and costs of downtime. Gamma irradiators require yearly resourcing to account for the decay of the cobalt isotope.
- **Operating costs** such as labor, electricity, water, energy source, and daily start-up validation.
- **Environmental impact** of ongoing irradiator operation.

²³⁷ For example, the Instructions For Use (IFU) included with medical products is typically a paper document, which may be dozens of pages long, placed inside the product packaging prior to sterilization. However, its orientation in the packaging can have a significant impact on the effectiveness of e-beam radiation.

- **Security costs and related actions** to meet federal and local regulations and to ensure maintenance of security through transport, use and decommissioning.
- **Decommissioning costs and environmental impact of decommissioning** of equipment, facility, and energy source.
- **Regulatory requirements** for initial and ongoing licensing, including inspection and decommissioning.
- **Supply chain and logistics** for optimal location of sterilization service center (including back-up facilities) versus in-house sterilization. It is important to note that the sterilization facility becomes an extension of the device's approval. Critical products may include primary and secondary sterilization facilities in their regulatory submissions.

Sterilization Technology Changes and Revalidation

A change or modification to a previously cleared device that could “significantly affect the safety or effectiveness of the device” requires resubmission for FDA 510(k) clearance. The FDA initially published guidance in 1997 to help medical device manufacturers determine when resubmission is warranted.²³⁸ In October 2017, the FDA published a substantially updated version of the 1997 guidance.²³⁹ The revisions preserve the basic format and content of the original while providing clarifying updates.

Regarding sterile devices, the FDA guidance notes that “when manufacturers make changes in sterilization methods, they must document that the important properties/specifications of the device remain unaffected” and that “manufacturers need to assess critically the need for a new 510(k) for their device in these instances.” Even when switching between established sterilization methods (such as from EtO to radiation), device manufacturers should consider any potential changes to material performance or biocompatibility to determine whether a new 510(k) submission for the device is warranted. In these assessments, the manufacturer should consider “known information on the sterilization, cleaning or disinfection method, its parameters, and the material being sterilized, cleaned, or disinfected, and determine if there are any new or significantly modified existing risks associated with using the proposed method.”²⁴⁰

If a manufacturer determines that the sterilization change does not “significantly affect the performance or biocompatibility of the device... it is unlikely a 510(k) is required as a result of this type of change.”²⁴¹ The guidance does not specifically address a change in the technology used for an established method, such as from one type of radiation sterilization technology to another. However, given the health and safety importance of sterilization, even a relatively minor sterilization process change—for example, a switch from one gamma facility to another without changes to packaging or dose—would require some level of documentation.²⁴²

²³⁸ U.S. Food and Drug Administration (FDA), “Deciding When to Submit a 510(k) for a Change to an Existing Device,” 510(k) Memorandum K97-1, issued January 10, 1997.

²³⁹ U.S. Food and Drug Administration (FDA), “Deciding When to Submit a 510(k) for a Change to an Existing Device,” Final Guidance, issued on October 25, 2017.

²⁴⁰ U.S. Food and Drug Administration (FDA), “Deciding When to Submit a 510(k) for a Change to an Existing Device,” Final Guidance, issued on October 25, 2017, page 27.

²⁴¹ Ibid.

²⁴² FNAL input.

If a device manufacturer determines that 510(k) resubmission is necessary due to changes in the sterilization process, it may typically submit a “Special 510(k).”²⁴³ This type of submission allows the applicant to provide more limited information than required for the original 510(k) submitted. The manufacturer instead describes the device modification and its impact, the risk analysis method used in the assessment, and the verification and/or validation activities determined to be necessary as a result. The submission also includes a declaration of conformity with design controls.²⁴⁴ Whereas the FDA averaged 173 calendar days for review of traditional 510(k) from 2012 to 2016, it averaged just 69 days for special 510(k) reviews averaged over the same timeframe.²⁴⁵

Without complete information about the performance of the materials in the two modalities ahead of time, much of the biocompatibility including: genotoxicity, sub-chronic and chronic, carcinogenicity, sensitization, implantation, extractability, and leachability. The durations for these sorts of tests each range from 6 weeks to 2 years, and costs for each range from \$3,000 to \$1 million.

As a result of these requirements, product revalidation considerations for manufacturers include:

- **Revalidation cost:** Eighty percent of medical device companies are small businesses. The initial cost of validation would have been included in their business plan, but the cost of repeating that effort may not be feasible once the product is established in the marketplace.
- **Functional equivalence:** To switch modalities, the device manufacturer must determine that the materials used in the device, along with its function, are unchanged by the new modality. The amount of freely available information on the performance of materials when subject to e-beam and x-ray is limited.
- **Regulatory approval:** Acquiring the necessary data for a regulatory submission requires approximately 6 months. Preparing the documentation for the regulatory submission takes another 6 months. Receiving the approval from all the necessary bodies can then take 1 to 4 years after submission. While it may be possible to obtain staggered regulatory approval, this would also result in staggered product rollouts, which may not be optimal for some manufacturers.

The cost and time related to these changes would vary depending on the medical device selected. However, it would likely be in the hundreds of thousands of dollars for each device impacted and exceed one year of elapsed time for all associated work and approvals.²⁴⁶

These factors help to explain why x-ray sterilization has not become more common in the United States despite its potential technical advantages. For example, beginning in 2013, a large, multinational contract sterilizer considered construction of two or more new x-ray processing facilities in the United States to provide medical device and consumer product sterilization services.²⁴⁷ The company believed that use of the

²⁴³ U.S. Food and Drug Administration (FDA), “The New 510(k) Paradigm Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications,” Final Guidance, issued March 20, 1998.

²⁴⁴ U.S. Food and Drug Administration (FDA), “Report on FDA’s Policy to be Proposed Regarding Premarket Notification Requirements for Modifications to Legally Marketed Devices,” Report to Congress, January 7, 2014.

²⁴⁵ Emergo Group, “How long it takes the U.S. FDA to clear medical devices via the 510(k) process: An examination of 15,000 medical device applications cleared by the U.S. Food and Drug Administration between 2012 and 2016,” Emergo Publication, March 2017, <https://www.emergogroup.com/resources>.

²⁴⁶ Gamma Industry Processing Alliance (GIPA), “Comparison of Cobalt-60 and X-Ray Technologies,” GIPA Fact Sheet, 2007, http://gipalliance.net/wp-content/uploads/documents/GIPAFactsheet_XrayComparison_000.pdf.

²⁴⁷ *Federal Trade Commission v. Steris Corporation*, No. 1:15 CV 1080, 2015 WL 5657294, (N.D. Ohio, September 24, 2015).

new technology would result in lower processing costs and more competitive prices for both existing and new customers.

Several challenges led to the termination of the initiative in 2015. To justify the roughly \$40 million investment in the initial two facilities, the company sought commitments from its existing United States customers to transition their products from gamma processing to the new x-ray sterilization service. However, despite projected cost-savings as high as 50 percent, the company was unable to obtain the customer commitments. Because the cost of sterilization relative to the overall cost of a sterilized device is estimated to be about 3 percent on average, the device manufacturers regarded the potential benefits as limited and insufficient to justify the cost and risk of transition. The costs cited by the companies included not only the costs related to product revalidation, but also the cost of assessing and addressing any further regulatory or business impacts the transition might entail.

In addition to challenges in obtaining the necessary customer commitments, the x-ray facility business model relied on certain power and capacity requirements of a combination e-beam/x-ray device that would be purchased for the project. However, the initial technical and cost estimates for the device proved to be overly optimistic. The revised estimates increased both the cost and risk of the x-ray facility development project.

Safety and Security Controls

Currently operational industrial gamma irradiator facilities are designed to meet standards developed by the IAEA and ANSI/HPS and must meet United States NRC design requirements under 10 C.F.R. Part 36, “Licenses and Radiation Safety Requirements for Irradiators.” The physical security of industrial gamma irradiators is also highly regulated²⁴⁸ under 10 C.F.R. Part 37, “Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material,” which includes requirements for background investigations; access controls; security plans; immediate detection, assessment, and response to unauthorized access; tracking of shipments;²⁴⁹ and security barriers; as well as other requirements. Security measures are incorporated into all aspects of the industry, including the design of the irradiators, the transportation of the sources, and the design, construction, operation, and maintenance of the facilities. The NRC initially estimated an average annual cost of approximately \$21,736 to maintain the Part 37 security requirements.²⁵⁰

All shipping casks used to transport Cobalt-60 in the United States must meet U.S. Department of Transportation (DOT) and NRC safety requirements. Sources transported to and from industrial irradiation facilities during reloading are shipped in large “Type B” transport casks designed according to stringent safety and security standards. A typical cobalt-60 finished source transport container, licensed to carry about 200,000 Ci of Cobalt-60, is approximately 1.5-m tall by 1.2-m diameter (5-ft tall by 4-ft diameter) and weighs many tons.

²⁴⁸ Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material, 10 C.F.R. § 37.

²⁴⁹ In the United States, safety and security responsibility during transport is taken on by the source manufacturer. The cost is often charged to the licensee under some sort of service contract.

²⁵⁰ U.S. Nuclear Regulatory Commission, “Rulemaking Issue Affirmation: Final Rule: Physical Protection of Byproduct Material (10 C.F.R. §§ 20, 30, 32, 33, 34, 35, 36, 37, 39, 51, 71, and 73),” (Washington D.C., December 2011, <http://www.nrc.gov/reading-rm/doc-collections/commission/secys/2011/2011-0170scv.pdf>).

Disposal Costs and Considerations

The large cobalt-60 sources used in the industrial scale irradiation facilities are typically used for 20 years from the date of purchase, although some facilities will keep sources longer if they have sufficient irradiator rack space. Most cobalt-60 manufacturers will accept return of sources under separately negotiated contracts. Disused irradiator sources remain highly radioactive and are handled and transported in the same manner as new cobalt-60 sources.

When return to the manufacturer is not possible, the source licensee is responsible for the safe and secure long-term management of these sources pending disposal. In such cases, the facility typically treats the used cobalt-60 in much the same way as spent nuclear fuel, storing the material under water until it has decayed to the point that it can be placed into dry storage containers within the facility perimeter. Lifecycle source tracking is used by suppliers and a number of regulators to ensure control and mitigate the risk that the source is abandoned. Cobalt-60 industrial irradiator sources are double-encapsulated in welded stainless steel that does not dissolve in water, enabling safe storage in a water pool for decades. Companies operating commercial gamma irradiators are required to provide a financial guarantee to the State (Agreement States) or Federal Government (NRC) for the costs of decommissioning the irradiator operator's facility, and disposition of the sources in it. This action is in accordance with the guidance provided under the IAEA Code of Conduct.

The return to manufacturer arrangements are currently available for most panoramic irradiator facilities. The source manufacturer typically recycles the decayed material by combining it with newly manufactured, very high activity cobalt-60 to create a new industrial irradiator source. For example, Nordion has recycled almost 20,000 cobalt-60 sources with a combined activity of almost 9 million Ci since it initiated recycling in 2003. The company expects to recycle thousands of additional sources with a combined activity of millions of Ci over the next several years. In addition to manufacturer recycling, a much smaller number of sources are purchased by specialty companies and re-encapsulated for use in smaller devices.

In the past, commercial disposal access challenges and security concerns related to high-activity sources has led on certain occasions to a temporary increase in government involvement, including the assumption of significant costs related to the disposal of sealed sources used in phytosanitary and food irradiators. However, the 2015 revised Concentration Averaging Branch Technical Position clarified the potential for currently operational "near-surface" disposal facilities to accept even the highest activity cobalt-60 sources as Class B waste.

Chapter 5: Alternative Technologies for Phytosanitary and Food-Safety Treatments

Introduction

A variety of methods are used to control the potentially harmful impacts of invasive pests and harmful pathogens in food products. These phytosanitary and food-safety treatments include chemical, extreme temperature, and radiation treatments of fresh produce transported between agricultural regions, as well as chemical and radiation treatments of plant, animal, and other food products for food-borne pathogen reduction. These methods may be used alone or in combination.²⁵¹ However, while chemical and extreme temperature technologies remain important for treatment of some products, for reasons described further below, they are not generally considered effective alternatives for the radioisotopic or non-radioisotopic radiation treatments.

Phytosanitary Treatment of Fresh Produce

Phytosanitary measures applied to fresh produce are used to prevent the spread between regions of invasive pests that may result from the transport of these goods. The most common insects of concern for the transport of fresh produce include fruit flies (family Tephritidae), butterflies and moths (order Lepidoptera), and mealybugs (family Pseudococcidae). Other important pest groups are scale insects, weevils, whiteflies, thrips, and mites.²⁵² Pre-harvest measures—such as crop inspection, management of survey traps, and the use of pesticides during the growing phase—help to ensure that quarantine pests are negligible in the final product. Other measures, including phytosanitary treatments, seek to eliminate or neutralize pests that remain on or inside the product after harvest. Phytosanitary treatment methods include cold, heat, chemical fumigation, and ionizing radiation.²⁵³

The phytosanitary treatment method employed by producers for a given product is subject to several constraints. It must effectively eliminate or neutralize the targeted pest while having a negligible negative impact on the product itself; it must be cost-effective; it must be acceptable from an environmental standpoint; and it must meet the specific requirements for the product at the consumer location.²⁵⁴

Chemical and extreme temperature phytosanitary treatment methods are aimed at pest mortality. They provide very high assurance that none of the pests residing on or inside the produce will survive the treatment process and establish themselves in the importing regions. Extreme cold and methyl bromide fumigation are the most common phytosanitary treatment methods.²⁵⁵ However, because methyl bromide

²⁵¹ Barkai-Golan, Rivka and Peter A. Follett, “Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce,” Academic Press/Elsevier (2017) provides a comprehensive overview of the use of radiation alone and in combination with other treatment methods to improve the safety and quality of fresh produce.

²⁵² Hallman, Guy J. and Carl M. Blackburn, “Phytosanitary Irradiation,” *Foods*, Vol. 5(1): 8 (2016). Barkai-Golan, Rivka and Peter A. Follett, “Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce,” Academic Press/Elsevier (2017).

²⁵³ Follett, Peter A. and Lisa G. Neven, “Current trends in Quarantine Entomology,” *Annual Review of Entomology*, Vol. 51: 359 (2006).

²⁵⁴ Hallman, Guy J., “Phytosanitary Measures to Prevent the Introduction of Invasive Species,” *Ecological Studies*, Vol. 193 (2007).

²⁵⁵ Hallman, Guy J., “Phytosanitary Applications of Irradiation,” *Comprehensive Reviews in Food Science and Food Safety*, Vol.10 (2011).

has been identified as an ozone-depleting substance, there has been increasing pressure to phase out its use as a phytosanitary treatment.²⁵⁶

Table 5.1: Subjective comparison of major phytosanitary treatments (after Hallman 2007)

Treatment	End point	Commodity tolerance	Cost	Certified organic	Speed	Logistics	Commonly treated commodity
Cold	Mortality	Moderate	Low	Yes	Very slow	Easy	Citrus, apple
Heated air	Mortality	Moderate	Moderate	Yes	Moderate	Moderate	Mango, papaya
Hot water immersion	Mortality	Moderate	Low	Yes	Fast	Moderate	Mango
Methyl bromide fumigation	Mortality	Moderate	Low	No	Fast	Easy	Citrus
Irradiation	Stop development	High	Moderate	No	Fast	Moderate	Mango, guava, pepper, lime

Domestic and international regulation of phytosanitary applications also has a significant impact on the methods and technologies employed. Phytosanitary requirements for United States imports and regional shipments are determined by the U.S. Department of Agriculture (USDA) and enforced by the USDA Animal and Plant Health Inspection Service (APHIS) in conjunction with its state partners. There are more than 150 domestic phytosanitary treatment facilities certified by the USDA both in the United States and overseas. These facilities treat potentially infested United States import and export products prior to shipment or upon arrival prior to distribution. In addition, certain products require disinfestation prior to shipment between United States agricultural regions, primarily between Hawaii and the United States mainland and between Florida and western states' agricultural regions.

Phytosanitary requirements for United States exports are typically determined in bilateral agreements between the United States and importing countries. However, because of their impact on international trade, phytosanitary treatment standards for many important trade commodities are addressed in multilateral trade agreements. Although United States law does not require domestic exporters to comply with foreign regulations, USDA facilitates the export of a wide range of United States agricultural products by working with foreign nations to administer an export certification program for United States producers. Under this program, phytosanitary inspection and certification of exports are provided to United States applicants based on the relevant treatment standard.²⁵⁷

²⁵⁶ Johnson, Judy A., Spencer S. Walse and James S. Gerik, "Status of Alternatives for Methyl Bromide in the United States," *Outlooks on Pest Management*, April 2012, DOI: 10.1564/23apr02.

²⁵⁷ Barkai-Golan, Rivka and Peter A. Follett, "Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce," Academic Press/Elsevier (2017).

Pathogen Reduction in Foods and Spices

The FDA regulates the safe production and distribution of food, including spices, in the United States, with the exception of meat and poultry, which are regulated by the USDA Food Safety Inspection Service (FSIS).²⁵⁸ Both agencies require food producers and importers to implement Hazard Analysis Critical Control Point (HACCP) programs. These programs use a systematic approach to identify and effectively address microbiological, chemical, and physical hazards in the food production and distribution process.²⁵⁹ Both agencies recognize a range of treatments that facilities can include in a Hazard Analysis and Risk-based Preventative Controls plan to address certain biological hazards. For example, the FDA identifies heat, high-pressure processing, antimicrobial fumigation (e.g., using EtO), and irradiation as potentially viable options.²⁶⁰ EtO treatment remains especially common as a means to reduce the incidence of microbial pathogens (e.g., salmonella) and the presence of molds and mycotoxins resident in spices.

As part of its efforts to encourage the increased use of pathogen reduction treatments in spices, the FDA has provided a survey and assessment of the current scientific literature comparing the effectiveness of treatment methods across the wide range of products and potential microbial risks, including EtO, steam, and ionizing radiation.²⁶¹ However, while the FDA and American Spice Trade Association urge spice manufacturers, importers, and distributors to include validated microbial reduction techniques as part of their HACCP or similar programs prior to product distribution, the FDA does not currently track the proportion of the total United States supply treated or the use of specific treatment methods; it does, however, track facilities. Acceptance of pathogen reduction treatment types among United States trading partners varies. For example, in the EU, EtO treatments are no longer approved, whereas the list of foods in many EU countries for which ionizing radiation is accepted as a pathogen reduction treatment has been expanding.²⁶²

Phytosanitary and Pathogen Reduction Treatment Options

Extreme Temperature Treatments

Exposure to cold is one of the oldest and most widely used phytosanitary treatments, involving sustained temperatures in the range of -0.6 to 3.3 °C (about 31 to 38 °F). A primary advantage of cold treatment is its tolerance by a wide variety of fruits, even those produced in tropical locations. The chief disadvantage is the long treatment times required, which range from 7 to 90 days, depending on the product and the pest targeted. As a result, some cold treatments are applied after packing during lengthy transport in ships. The relatively long treatment periods may also constitute a business risk in the case of power outage or

²⁵⁸ As described below, the USDA Animal and Plant Health Inspection Service (APHIS) regulates the distribution and phytosanitary treatment of fresh produce to prevent the transport of invasive insect pests between agricultural regions.

²⁵⁹ For example, under the 2011 Food Safety Modernization Act (FSMA), food manufacturers regulated by the FDA are required to develop and implement a Hazard Analysis and Risk-based Preventive Controls (HARPC) plan, which includes (1) an evaluation of the potential food-safety hazards at the facility; (2) identification of preventive controls to significantly reduce or eliminate the identified hazards; (3) specification of a method to verify and document that facility implementation of process controls remain effective; (4) if applicable, a program to ensure that potential hazards originating elsewhere in the product supply chain are addressed; and (5) specification of corrective actions, including a recall plan, the facility will take if problems arise. (21 C.F.R. § 117 “Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food.”) The USDA-FSIS HACCP program requirements for meat and poultry producers are similar. (U.S. Department of Agriculture Food Safety and Inspection Service, “Pathogen Reduction; Hazard Analysis and Critical Control Point (HACCP) Systems; Final Rule,” 9 C.F.R. § 304, et al., *Federal Register*, Vol. 61, No. 144, Thursday, July 25, 1996, 38805-38989.)

²⁶⁰ U.S. Food and Drug Administration (FDA), “Hazard Analysis and Risk-Based Preventive Controls for Human Food: Guidance for Industry,” Draft Guidance, January 18, 2018.

²⁶¹ U.S. Food and Drug Administration (FDA), “Risk Profile: Pathogens and Filth in Spices,” Center for Food Safety and Applied Nutrition, 2017.

²⁶² Pillai, Suresh D. and Shima Shayanfar, “Electron Beam Technology and Other Irradiation Technology Applications in the Food Industry,” in Topical Collection “Applications of Radiation Chemistry,” edited by Margherita Venturi, Mila D’Angelantonio; *Topics in Current Chemistry* (2) (2017) 375:6; DOI 10.1007/s41061-016-0093-4.

equipment failure. For some products a treatment interruption that leads to an increase in temperature as little as 1 °C, even for a short period of time, could require the process to be restarted.²⁶³

Heated-air phytosanitary treatments use temperatures as high as 52 °C (approximately 125 °F) to kill pests in or on the targeted product, primarily fresh fruits. The speed of treatment varies depending on a wide range of factors, including the product and product packaging, the facility size and design, and the humidity present in the air at the facility location. For resilient products, high-temperature treatments may enable shorter treatment time periods, with some treatments lasting as little as 3 hours. These applications force heated air through a shipment to achieve relatively fast and uniform exposure. Less-resilient products may require slower exposure, which consists of circulating heated air through the treatment chamber, gradually and slowly penetrating the product. Heated-air treatments are one of the most challenging phytosanitary treatments to manage because many variables may affect their efficacy. For example, faster, forced-air treatments might damage treated commodities, while slower applications could fail if pests are able to acclimate to the increasing temperature through “heat-shock proteins.”²⁶⁴

Steam treatments are often used for pathogen reduction in spices and certain food products. For example, canned foods are rendered commercially sterile using pressurized, saturated steaming of products packed into a steam chamber. Microbial death occurs based on numerous factors including the time and temperature of treatment and thermal resistance characteristics of the target organism.²⁶⁵ In steam treatment of spices, lethality arises from the exposure of spice microflora to steam for adequate times and at sufficient temperatures, and may or may not include pressure or steam saturation.²⁶⁶

The two basic methods used for steam treatment of spices are batch and continuous processing. In batch processing, packages of spices are palletized and loaded into a treatment chamber, followed by steam injection into the chamber with or without pressure. Continuous steam processing involves equipment designed to continually move spice through a system where steam is injected into the unpackaged product. Due to variations in bulk density among spices (as well as other factors such as packing permeability and stacking configuration), there is no set of conditions for steam treatments that is effective for all spices. Processors must determine treatment parameters that ensure steam penetration throughout the package for an adequate time period to sufficiently reduce the targeted pathogens.

Chemical Treatments

Methyl Bromide Fumigation

Methyl bromide fumigation is by far the most common phytosanitary treatment method in the United States. The USDA lists approximately 130 facilities in the United States that provide methyl bromide phytosanitary services.²⁶⁷ These facilities treated more than 200 metric tons of fresh fruits and vegetables in 2010.²⁶⁸ Despite increased regulatory costs across the past several decades, the method remains highly cost-effective. The chemical itself is inexpensive and the process can be performed in simple facilities. The

²⁶³ Hallman, Guy J., “Phytosanitary Measures to Prevent the Introduction of Invasive Species,” *Ecological Studies*, Vol. 193 (2007).

²⁶⁴ Ibid.

²⁶⁵ U.S. Food and Drug Administration (FDA), “Updated FDA Risk Profile: Pathogens and Filth in Spices (2017),” February 2018 released, <https://www.fda.gov/downloads/Food/FoodScienceResearch/RiskSafetyAssessment/UCM581362.pdf>.

²⁶⁶ Ibid.

²⁶⁷ U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), “FDA APHIS Approved Treatment Facilities,” August 5, 2018, https://www.aphis.usda.gov/import_export/plants/manuals/ports/downloads/national_treatment_facility_list.pdf.

²⁶⁸ Johnson, Judy A., Spencer S. Walse and James S. Gerik, “Status of Alternatives for Methyl Bromide in the United States,” *Outlooks on Pest Management*, April 2012, DOI: 10.1564/23apr02.

primary consideration in facility design is construction of leak-tight fumigation chambers. Methyl bromide treatment time requirements are short, most lasting less than 2 hours.²⁶⁹

Methyl bromide fumigation may also be combined with other treatments; for example, it may precede or follow extreme-cold treatment. Certain commodities may not tolerate treatment using heat or cold alone to the degree necessary for complete phytosanitary control but can tolerate multiple treatment types applied sequentially. Cost also plays a role: For example, it may be cost effective for a producer to apply a partial cold treatment during transit by ship, followed by a reduced methyl bromide fumigation prior to distribution.²⁷⁰

The primary disadvantage of methyl bromide fumigation is that the chemical has long been recognized as a significant ozone-depleting substance and its use for non-critical applications has been phased out as the result of international agreements. Although post-harvest phytosanitary uses have been indefinitely exempted from these restrictions, there remains domestic and international pressure to reduce its use. As a result of these considerations, the USDA actively encourages the use of alternatives, including ionizing radiation, for phytosanitary treatments when feasible.²⁷¹ The commercial availability of recapture systems and the development of processes to contain, destroy, or reuse methyl bromide after use to reduce the negative impacts have not altered the USDA stance on the treatment.²⁷²

Ethylene and Propylene Oxides

EtO and propylene oxide (PPO) are the two chemicals most commonly used to sanitize foods such as nutmeats, dried herbs, dried fruit, and spices. These treatments achieve pathogen reduction through the highly potent chemical interaction of the EtO or PPO molecules with proteins and DNA in the contaminant microorganisms resident on the targeted product. These chemical interactions disrupt and damage cell structures, ultimately resulting in the destruction of the microorganisms.²⁷³ However, these chemicals are toxic and flammable prior to use, presenting potential environmental, health, and safety concerns. Therefore, they are largely used to treat foods (as well as non-food products) that are not conducive to extreme temperature or radiation treatments.²⁷⁴

Ionizing Radiation

Gamma rays, x-rays, and e-beams function in a broadly similar way to achieve insect lethality and sterilization: Ionizing radiation disrupts normal cellular function in pests by breaking chemical bonds within DNA and other biomolecules.²⁷⁵ Exposure to radiation causes both direct and indirect damage in biological systems. The direct effects arise from the ionization, as electrons are removed from biologically important molecules, such as DNA, RNA, or proteins. The indirect effects arise from the free radicals formed during the ionization of water molecules within the biological systems. These free radicals cause a variety of additional

²⁶⁹ Hallman, Guy J., "Phytosanitary Measures to Prevent the Introduction of Invasive Species," *Ecological Studies*, Vol. 193 (2007).

²⁷⁰ Ibid.

²⁷¹ Pillai, S. and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," *Global Safety of Fresh Produce: A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014).

²⁷² Johnson, Judy A. Spencer S. Walse and James S. Gerik, "Status of Alternatives for Methyl Bromide in the United States," *Outlooks on Pest Management*, April 2012, DOI: 10.1564/23apr02.

²⁷³ Mendes, Gisela C. C., Teresa R. S. Brandao, and Cristina L. M. Silva, "Ethylene oxide sterilization of medical devices: A review," *American Journal of Infection Control*, November 2007, Volume 35, Issue 9, Pages 574–581.

²⁷⁴ National Research Council National Academies, "Acute Exposure Guideline Levels for Selected Airborne Chemicals," Volume 9 (2010).

²⁷⁵ Barkai-Golan, Rivka and Peter A. Follett, *Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce*, Academic Press/Elsevier (2017); Guy J. Hallman and Carl M. Blackburn, "Phytosanitary Irradiation," *Foods*, 2016, 5, 8; doi:10.3390/foods5010008; Follett, Peter, "Phytosanitary Irradiation for Fresh Horticultural Commodities: Generic Treatments, Current Issues, and Next Steps," *Stewart Postharvest Review* (2014).

damaging effects in organisms. Because radiotolerance varies between taxonomic groups of insects and among insect life stages, the most effective radiation dose also varies among treated products.²⁷⁶

Regardless of food type or application, the FDA regulates the use of radiation on foods as a “food additive,” with oversight of its use shared between the FDA and USDA.²⁷⁷ The FDA has determined that gamma, x-ray, and e-beam are equally safe and effective for approved food irradiation treatments, including both pathogen reduction and phytosanitary applications. FDA rules permit gamma source treatments using either cobalt-60 or cesium-137, e-beam radiation up to 10 MeV, and x-ray radiation up to 7.5 MeV.²⁷⁸ Similarly, the most prominent international food safety standards also consider the primary radiation sources to be equally safe and effective for approved treatments. The Codex Alimentarius, jointly maintained under the Food and Agriculture Organization (FAO) of the United Nations (UN) and the World Health Organization (WHO), has approved the use of gamma radiation using cobalt-60 and cesium-137 sources and e-beam radiation up to 10 MeV, but maintains a maximum energy for x-ray treatments at 5 MeV.²⁷⁹

Despite these standards, there is significant variation among countries regarding the acceptable use of different radiation sources for phytosanitary, pathogen reduction, and other food treatment products. In 2014, the FAO and IAEA initiated a Coordinated Research Project (CRP) on the “Development of Electron Beam and X-Ray Applications for Food Irradiation.”²⁸⁰ The CRP objective is to “accelerate development and facilitate implementation of practical techniques for the irradiation of food and agricultural products using e-beam and x-ray through the establishment of an international collaborative network.”²⁸¹ Among its research topics is an increase in the x-ray maximum energy to 7.5 MeV. The research timeline includes an ongoing series of research projects and CRP workshops leading to publication of project results and conclusions in 2020.²⁸²

Primary Food Irradiation Applications

For the purposes of this chapter, food irradiation applications can be generally classified into two groups:

- Low dose irradiation, from 100 Gy to 1,000 Gy, is used for the phytosanitary treatment of fresh produce. These applications depend largely on pest sterility, but not lethality, to prevent the spread of potentially invasive pests among geographic regions. Low-dose irradiation may also be used for product quality applications, such as sprout inhibition in susceptible foods (such as potatoes, onions, and garlic), to delay ripening in fresh fruits and vegetables, and to extend the shelf life of fresh produce. In the United States, doses up to 500 Gy are approved for treatment of stored wheat and wheat flour.²⁸³

²⁷⁶ Follett, Peter, “Phytosanitary Irradiation for Fresh Horticultural Commodities: Generic Treatments, Current Issues, and Next Steps,” *Stewart Postharvest Review*, 2014, 3:1.

²⁷⁷ *The Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act* (FD&C Act) of 1958 places food irradiation under the food additive regulations in 21 C.F.R. § 179.

²⁷⁸ FDA rules allow x-ray radiation to up to 7.5 MeV when tantalum or gold is used as the electron beam target in the device, which is nearly always the case. If alternative target materials are used in the device, the rules maintain a 5 MeV limit on x-ray applications. 21 C.F.R. § 179, Subpart B: Radiation and Radiation Sources.

²⁷⁹ Codex Alimentarius, “General Standard for Irradiated Foods,” Codex Stan 106-1983, Rev.1-2003.

²⁸⁰ FAO / IAEA Division of Nuclear Techniques in Food and Agriculture, “Development of Electron Beam & X-ray Applications for Food Irradiation: Report of the First Research Coordination Meeting,” CRP D61204, Meeting D61024-CR-1, Vienna, Austria, 19 – 23 October 2015, <http://www-naweb.iaea.org/nafa/fep/crp/fep-xray-application-food-irradiation.html>.

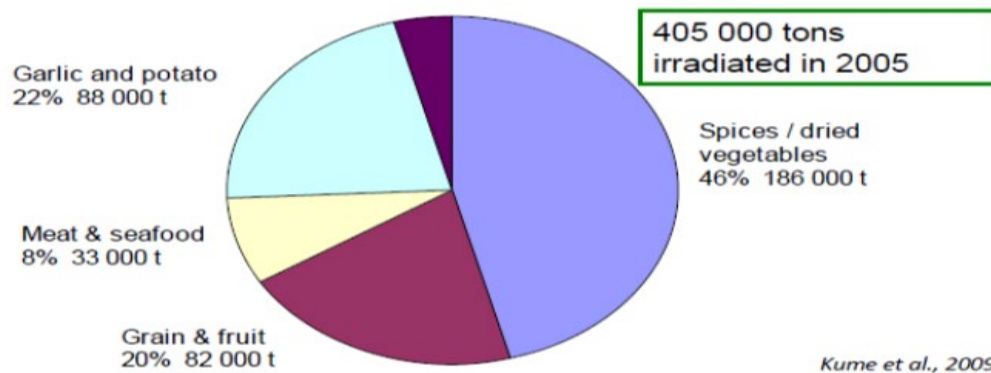
²⁸¹ Ibid.

²⁸² Ibid.

²⁸³ Hallman, Guy J., “Control Of Stored Product Pests By Ionizing Radiation,” *Journal of Stored Products Research*, 52 (2013).

- Medium and high dose irradiation, ranging from 1,000 to 100,000 Gy, is used for food sanitation. These treatments inactivate microbial pathogens responsible for foodborne infections in uncooked meat and poultry products, raw oysters, seeds, lettuce, and spinach, as well as certain food additives like spices, enzyme preparations, natural gum, and other ingredients.²⁸⁴ The FDA has approved the use of up to 8,000 Gy for the control of microbial pathogens on seeds for sprouting, and up to 30,000 Gy for the microbial disinfection of spices.²⁸⁵

Figure 5.1: Irradiated Foods – Quantities Worldwide²⁸⁶



Phytosanitary irradiation (PI) has been in continuous use in the United States since 1995 when papaya and other tropical fruits were shipped from Hawaii to Illinois to be irradiated for sale on the United States mainland. In 1999, irradiation of Florida produce for wider domestic markets began, starting with guava and followed by sweet potato and other fruits in subsequent years. In 2000, an x-ray facility became operational in Hawaii, irradiating the products previously shipped to the mainland for treatment. This facility was the first dedicated to treatment of fresh produce and now has export approvals for 25 fruits and vegetables to the United States mainland.²⁸⁷ In 2014, the facility was responsible for irradiating approximately 4,500 tons for shipment to the mainland United States. Irradiation is the only phytosanitary treatment approved by the USDA for 16 commodities produced in Hawaii and transported to markets on the United States mainland, as well as for at least six high volume fresh fruit commodities imported from Mexico.²⁸⁸

²⁸⁴ Pillai, S. and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," in *Global Safety of Fresh Produce, A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014), page 227-228.

²⁸⁵ Barkai-Golan, Rivka and Peter A. Follett, *Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce*, Academic Press/Elsevier (2017).

²⁸⁶ Pillai, Suresh, "Justification for Irradiation Technologies," Texas A&M University, 2017.

²⁸⁷ Barkai-Golan, Rivka and Peter A. Follett, *Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce*, Academic Press/Elsevier (2017).

²⁸⁸ Pillai, S. and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," in *Global Safety of Fresh Produce – A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014); Hallman, Guy J. and Paisan Loaharanu, "Phytosanitary Irradiation – Development and Application," *Journal of Radiation Physics and Chemistry, Radiat. Phys. Chem* (2016), <http://dx.doi.org/10.1016/j.radphyschem.2016.08.003>.

Table 5.2: Tons of produce irradiated in the United States for phytosanitary purposes in the United States in 2014²⁸⁹

Location	Gamma	E-Beam	X-Ray
Hawaii	2,000		4,500
Rest of United States	500	200	

A primary advantage of irradiation as a phytosanitary treatment is that it has no or negligible effects on commodity quality.²⁹⁰ Fresh commodities, fruits in particular, tolerate irradiation better than alternative treatments such as heat, cold, and chemical fumigation.²⁹¹ Collateral benefits of irradiation of fresh fruit and vegetable products include the extension of shelf life and the potential to reduce spoilage-inducing pathogens in fresh-food products.²⁹²

Historically, food irradiation has been stigmatized, primarily among retailers, who feared that specific labeling required for irradiated foods may mistakenly be interpreted by consumers as a warning.²⁹³ In the United States, irradiated foods or fresh horticultural products must be labeled as “treated by irradiation” alongside a radura symbol.²⁹⁴ No other PI treatment type requires labeling or treatment identification. Irradiated foods cannot be USDA-certified organic as a result of the treatment. Despite these requirements, the stigma attached to radiation has significantly, if not entirely, eroded.²⁹⁵ Irradiated foods are generally accepted by consumers and sell well.²⁹⁶

Primary Food Irradiation Sources

All three types of food (and multipurpose) irradiation facilities have a similar layout, including typical warehouse features, such as loading dock access, product conveyance mechanisms, and areas for temporary storage. All three types also feature a highly shielded bunker where products are exposed to the radiation source. However, in contrast to the targeted radiation emitted by x-ray and e-beam devices, cobalt-60 sources emit radiation in all directions. As a result, gamma food irradiation typically involves conveyance of packaged products around a rack of cobalt-60 sources located in the center of the bunker. Depending on

²⁸⁹ Henon 2015 presentation (IAEA).

²⁹⁰ Barkai-Golan, Rivka and Peter A. Follett, *Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce*, Academic Press/Elsevier (2017).

²⁹¹ Hallman, Guy J. and Paisan Loaharanu, “Phytosanitary Irradiation – Development and Application,” *Journal of Radiation Physics and Chemistry, Radiation Physics and Chemistry* (2016), <http://dx.doi.org/10.1016/j.radphyschem.2016.08.003>.

²⁹² Since ionizing radiation does not target just one biological entity, the reduction in spoilage organisms and possible pathogens is purely collateral in nature. Shayanfar, S., K. Mena and S.D. Pillai, “Quantifying the Reduction in Potential Health Risks from Non O157 Shiga Toxin Producing Escherichia Coli in Strawberries by Electron Beam Processing,” *Food Control*, 72: 324-327 (2017).

²⁹³ Follett, P.A. and E.D. Weinert, “Phytosanitary irradiation of fresh tropical commodities in Hawaii: Generic treatments, commercial adoption, and current issues,” *Radiation Physics and Chemistry*, 81 (2012) 1064–1067.

²⁹⁴ Ibid.

²⁹⁵ IAEA, “Development of New Applications of Machine Generated Food Irradiation Technologies: Report of a Consultant Meeting on a Proposed Coordination Research Project,” IAEA Headquarters, Vienna, Austria 26-30 May 2014 (2015), page 4.

²⁹⁶ Hallman, Guy J. and Carl M. Blackburn, “Phytosanitary Irradiation,” *Foods*, 2016, 5, 8; doi:10.3390/foods5010008; Peter B. Roberts and Yves M Henon, “Consumer Response to Irradiated Food: Purchase versus Perception,” *Stewart Postharvest Review*, Vol. 3:5 (2015.)

the facility configuration, packaged products make a single pass or multiple passes around the source rack in order to obtain the prescribed dose.

Isotopic Sources (Cobalt-60)

Gamma irradiation is the predominant phytosanitary irradiation technology in commercial use. There are three gamma facilities in the United States certified by the USDA for PI applications. The Pa'ina facility in Hawaii and Gateway America in Mississippi are dedicated food irradiation facilities. In addition to PI, Gateway is also approved by the USDA to irradiate red meat, poultry, oysters, crustaceans and certain other types of seafood to reduce harmful bacteria. Sterigenics operates a multipurpose gamma facility in Florida, capable of providing both food and nonfood irradiation services.²⁹⁷

Because gamma rays can effectively penetrate large bulky materials, gamma radiation can be used to treat relatively large loads of packaged product with a sufficiently uniform dose to remain within the parameters required for phytosanitary treatment. Regardless, the low treatment doses and uniform dose distributions required for phytosanitary irradiation treatments may pose processing challenges for large, multipurpose industrial irradiation facilities using cobalt-60.²⁹⁸ The 1,000 Gy maximum dose for PI is 25 to 50 times lower than doses used in medical device sterilization and 100 times lower than doses used for some materials processing applications.²⁹⁹

The source racks used for gamma PI typically utilize millions of Ci of cobalt-60. Because cobalt-60 sources constantly generate radiation, operations are initiated or ceased by moving the source rack into or out of a shielded containment area located underneath the processing chamber. In “dry storage” configurations this containment area is a shielded pit. In “wet storage” facilities it is a shielded pool of water. Typical dose rates for gamma treatments are about 100 Gy per minute.³⁰⁰

Electron Beam Accelerators

Although accelerator technologies vary, all use electricity to generate and accelerate a beam of electrons at the target. However, in contrast to the photon energy generated by both gamma sources and x-ray technologies, the electron energy produced through linear acceleration has a relatively short range and less ability to penetrate treated products. E-beam penetration is primarily a function of the accelerator energy and the areal density of the target, a measure which takes into consideration both the size and weight of the packaged product.³⁰¹ As a result, the size and density distribution of the processing containers and products are particularly important considerations for achieving the required dose uniformity. In addition, e-beam facilities may irradiate containers from two opposing sides by flipping or rotating the processing containers for a second exposure or by using two accelerators to irradiate both sides of the product simultaneously.

²⁹⁷ Hallman, Guy J., Yves M. Hénon, Andrew G. Parker, and Carl M. Blackburn, “Phytosanitary irradiation: An overview,” 2016 — Florida Entomologist — Volume 99, Special Issue 2 (2016).

²⁹⁸ Hallman, Guy J., Yves M. Hénon, Andrew G. Parker, and Carl M. Blackburn, “Phytosanitary irradiation: An overview,” 2016 — Florida Entomologist — Volume 99, Special Issue 2 (2016). Follett, P.A. and E.D. Weinert, “Phytosanitary irradiation of fresh tropical commodities in Hawaii: Generic treatments, commercial adoption, and current issues,” Radiation Physics and Chemistry 81 (2012) 1064–1067.

²⁹⁹ Cokragan, Ahmet, “Commercial Use of Phytosanitary Irradiation,” MEVEX presentation Toluca, Mexico, October 14, 2015.

³⁰⁰ Pillai, S., “Principles of Ionizing Radiation and eBeam and X-ray Dose Deposition,” Texas A&M E-Beam Workshop, Texas A&M University, (2017).

³⁰¹ Ibid.

E-beam technologies are relatively energy efficient, converting approximately 10 percent to 50 percent of the electricity input into beam energy depending on the age and efficiency of the system.³⁰² Furthermore, some e-beam devices can provide a range of electron energies, which can improve the efficiency and effectiveness of processing a range products. Some devices also can switch between e-beam and x-ray generation, and the new generation of linacs can customize energy and power for different applications. The USDA has certified two e-beam facilities for phytosanitary treatment in the United States. Both the National Center for Electron Beam Research in Texas and Sadex in Iowa are multipurpose service centers that irradiate a variety of consumer products, including food.

X-ray Devices

X-rays generated for industrial scale applications, including food treatment, typically utilize a 5 MeV to 10 MeV e-beam accelerator with at least 80 kW of power to strike a tungsten or tantalum target with a high energy beam of electrons.³⁰³ The collision of the accelerated electrons with the heavy-metal target produces x-rays in the form of bremsstrahlung radiation. This radiation is comprised of photon energy, which impacts targeted products in a similar manner as the photon energy produced by cobalt-60. However, while cobalt-60 gamma rays are produced at specific and discrete energies (1.17 MeV and 1.33 MeV), bremsstrahlung radiation is comprised of a broad spectrum of energies, ranging as high as the electron accelerator that produced them, but with an average energy about one third of the maximum.

The penetration of x-rays and cobalt-60 gamma rays are similar, although the potentially higher energy x-ray photons—typically generated at 5 to 7.5 MV—should result in an even more uniform dose distribution relative to the 1.25 MeV average energy generated by cobalt-60.³⁰⁴ For industrial-scale gamma irradiation, DURs are typically about 1.6.³⁰⁵ Commercial arrangements using x-rays and loads narrower than the dimensions of a standard pallet have achieved DUR under 1.3.³⁰⁶ However, because phytosanitary treatments are subject to relatively low maximum dose requirements relative to pathogen reduction treatments, achievement of a relatively low DUR is necessary for phytosanitary irradiation to be effective.³⁰⁷

X-ray PI has a very large energy requirement. In contrast to the relatively efficient generation of an e-beam from electricity, the conversion of electrical energy into x-rays is highly inefficient, with approximately 92 percent of the e-beam energy lost in the conversion process in a 5 MeV machine. At higher energies, the energy conversion rate of x-rays improves from roughly 8 percent to about 12 percent in a 7.5 MeV device. The higher energy also increases the rate at which products can be treated.³⁰⁸ Regardless, by one estimate, x-ray facilities consume 10 times more electricity than e-beam facilities to deliver the same dose to the

³⁰² Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (IIA), “A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products,” (2017).

³⁰³ Ibid.

³⁰⁴ International Atomic Energy Agency, “Manual of Good Practice in Food Irradiation,” Technical Reports Series No. 481 (2015).

³⁰⁵ The dose distribution can be expressed in terms of a dose uniformity ratio (DUR), which is the ratio between the maximum dose and minimum dose received by an irradiated target. Ratios closer to 1 indicate small variation in dose throughout the target, while ratios further from 1 indicate a greater difference between the highest and lowest dose areas within the irradiated product.

³⁰⁶ Hallman, Guy J., “Phytosanitary Applications of Irradiation,” *Comprehensive Reviews in Food Science and Food Safety*, Vol.10 (2011); Guy J. Hallman and Carl M. Blackburn, “Phytosanitary Irradiation,” *Foods*, 2016, 5, 8; doi:10.3390/foods5010008. Follett, P.A. and E.D. Weinert, “Phytosanitary irradiation of fresh tropical commodities in Hawaii: Generic treatments, commercial adoption, and current issues,” *Radiation Physics and Chemistry* 81 (2012) 1064–1067.

³⁰⁷ For example, based on the most common minimum dose of 400Gy and the regulatory maximum of 1000Gy, a DUR below 2.5 would be likely be required, which would likely result in a DUR target closer to 2 for quality assurance purposes. Brown, David, Mevex Corporation, “The Truth About Radiation Processing: ‘Niche Markets... Hidden Gems’” presented at the 2016 Texas A&M Electron Beam Workshop.

³⁰⁸ International Atomic Energy Agency, “Manual of Good Practice in Food Irradiation,” Technical Reports Series No. 481 (2015).

product, although the comparative performance will vary depending on the specific devices and operational factors considered.³⁰⁹

Technology Selection Considerations

The following section outlines potential replacement considerations, including the ability of the technology to meet the application requirements, as well as the cost, and security factors of each technology.

Domestic and International Regulation of Phytosanitary Irradiation

Phytosanitary irradiation, which relies on lower doses than pathogen reduction treatments, provides quarantine security in large part by rendering resident pests sterile. As a result, the presence of live quarantine insects in the treated product is not an indication that the treatment was unsuccessful. However, the presence of live, even if sterile, insects in effectively treated products has been a challenge for the use of radiation to treat cross-border trade commodities, which generally rely on physical inspection of shipments for the elimination of live insects to confirm that the quarantine treatment has been effective. Instead, confidence in phytosanitary irradiation as an effective quarantine treatment relies upon indirect factors, including confidence in the research supporting the required minimum dose, confidence in the process controls applied during dose application, and confidence in the measures taken after treatment to prevent re-infestation.³¹⁰

In 2006, USDA approved “generic” radiation quarantine treatments to control a wide range of common insect pests. A generic treatment dose is a single dose of radiation determined to effectively control a broad group of pests in a range of products, without adversely affecting the quality of the commodities, and without having to test each product and pest combination separately.³¹¹ As a result, treatment standards may be generic for entire food groups and multiple risk factors (i.e., invasive pest types), not just for individual food items or specific risk agents, as is the case with other treatment methods.³¹² The 2006 USDA rule identifies minimum radiation doses of 150 Gy for any tephritid fruit fly and 400 Gy for all other insects, with certain, narrow exceptions, and 23 specific non-insect pests.³¹³ The USDA standards apply to all fresh horticultural commodities. As a result, if a pest risk assessment for a fresh horticultural product demonstrates that the excepted pest is not associated with the commodity, no further research is necessary for the generic treatment to receive approval.³¹⁴ Furthermore, application of these generic treatments may address new combinations of commodity and pest that arise in the future, further increasing the cost-effectiveness of radiation treatments relative to other methods.³¹⁵

³⁰⁹ Brown, Tony, “Mevox Equipment for Phytosanitary Irradiation,” Mevox Corporation, presentation delivered at Chapman University, 2016, <https://www.chapman.edu/scst/files/news-and-events/phytosanitation-irradiation-16/brown.pdf>.

³¹⁰ Hallman, Guy J. and Paisan Loaharanu, “Phytosanitary Irradiation – Development and Application,” *Journal of Radiation Physics and Chemistry*, Radiat. Phys. Chem (2016), <http://dx.doi.org/10.1016/j.radphyschem.2016.08.003>.

³¹¹ Follett, Peter “Phytosanitary Irradiation for Fresh Horticultural Commodities: Generic Treatments, Current Issues, and Next Steps,” *Stewart Postharvest Review*, 3:1 (2014).

³¹² Hallman, Guy J. , “Process Control in Phytosanitary Irradiation of Fresh Fruits and Vegetables as a Model for Other Phytosanitary Treatment Processes,” *Food Control*, (2016).

³¹³ The exceptions are the pupa and adult stages of Lepidoptera (moths and butterflies). Peter Follett, “Entomology and the Evolution of Generic Doses.” Presentation, Eighth Annual Phytosanitary Irradiation Forum, June13-15, 2018.

³¹⁴ Follett, Peter, “Phytosanitary Irradiation for Fresh Horticultural Commodities: Generic Treatments, Current Issues, and Next Steps,” *Stewart Postharvest Review* (2014).

³¹⁵ Hallman, Guy J. , “Process Control in Phytosanitary Irradiation of Fresh Fruits and Vegetables as a Model for Other Phytosanitary Treatment Processes,” *Food Control*, (2016).

The FDA and USDA have also approved radiation dose limits for pathogen reduction for a range of foods as shown in Table 3.3 below. However, the total quantity of foods and spices irradiated in the United States is difficult to ascertain. By one estimate, approximately 18 million pounds of ground beef is commercially irradiated in the United States for retail and commercial sales, with roughly half treated at e-beam facilities.³¹⁶

Table 5.3: List of Food and Food Items permitted for ionizing radiation treatment in the United States, C.F.R. Part 1779.25(b)

Food/Food-Related Item	Specific Application	Maximum Allowable Dose (kGy)
Fresh, non-heated processed pork	Pathogen control	0.3-1.0
Fresh/frozen uncooked poultry products	Pathogen control	3
Refrigerated, uncooked meat products (sheep, cattle, swine, and goat)	Pathogen control	4.5
Frozen uncooked meat products (sheep, cattle, swine, and goat)	Pathogen control	7
Fresh/frozen molluscan shellfish	Pathogen control	5.5
Fresh shell eggs	Pathogen control	3.0
Dry or dehydrated spices and food seasonings	Microbial disinfection	30
Fresh produce	Growth and maturation inhibition	1
Fresh produce	Insect disinfestation	1
Fresh lettuce and fresh spinach	Pathogen control	4.0
Seeds for sprouting	Pathogen control	8.0
Dry/dehydrated species and food seasonings	Microbial disinfection	30
Dry/dehydrated enzyme preparations	Microbial disinfection	10
Wheat flour	Mold control	0.5
White potatoes	Inhibit sprouting	0.15

As domestic and international efforts to phase out methyl bromide fumigation continue, irradiation may be an acceptable phytosanitary treatment replacement option in many cases. The Treatment Quality Assurance Unit (TQAU) within USDA/APHIS, working with domestic and international partners, has led an effort to enable the use of ionizing irradiation as a phytosanitary treatment for internationally traded horticultural products through development of the regulatory and technical infrastructure necessary to support its use. The use of ionizing radiation for phytosanitary treatments has increased by an estimated 10 percent each year since 2000, as countries have approved its use for an increasing number of products and pests.³¹⁷ USDA expects the use of irradiation as a phytosanitary treatment to increase further as methyl bromide is phased out.³¹⁸ The ability to employ a generic treatment dose to new invasive pest and commodity combinations as they emerge has the potential to improve the cost-efficiency of phytosanitary irradiation treatments relative to other methods.

³¹⁶ Pillai, S. and Shima Shayanfar, "Electron Beam Technology and Other Irradiation Technology Applications in the Food Industry," in Topical Collection "Applications of Radiation Chemistry," Top Curr Chem (Z) (2017) 375:6; DOI 10.1007/s41061-016-0093-4.

³¹⁷ Hallman, Guy J. and Carl M. Blackburn, "Phytosanitary Irradiation," Foods, 2016, 5, 8; doi:10.3390/foods5010008.

³¹⁸ United States Department of Agriculture: Animal and Plant Health Inspection Service, "CPHST: Treatment Technology," webpage accessed March 28, 2017, https://www.aphis.usda.gov/aphis/ourfocus/planthealth/ppq-program-overview/cphst/sa_projects/ct_commodity-treatments.

The International Plant Protection Convention (IPPC), administered under the United Nations Food and Agriculture Organization is the most widely recognized standard-setting organization for phytosanitary measures. The organization facilitates the implementation of the phytosanitary treatment areas of the World Trade Organization Agreement on Sanitary and Phytosanitary Measures (SPS) and similar agreements. The IPPC's 182-member nations coordinate treatment standards and associated policies and programs through the annual Commission on Phytosanitary Measures (CPM) and its subsidiary and oversight bodies.³¹⁹

The IPPC has agreed upon phytosanitary irradiation treatment standards for 13 common pests, as well the 150 Gy generic treatment standard that applies to most fruit flies.³²⁰ Regardless of the fact that although the IPPC rejected the 400 Gy generic standard adopted by the USDA, it is the one used for ~95 percent of all commodities irradiated for phytosanitary purposes.³²¹ USDA and IPPC phytosanitary standards treat all three types of radiation processing equally.

The USDA-APHIS has concluded bilateral phytosanitary irradiation agreements, called Framework Equivalency Work Plans, with Australia, the Dominican Republic, Ecuador, Ghana, India, Laos, Malaysia, Mexico, Pakistan, Peru, the Philippines, South Africa, Thailand, and Vietnam. These agreements stipulate that each country will legally accept the other's system of irradiated products.³²² Most irradiated produce imports to the United States are treated in USDA-certified "preclearance" facilities in or near their country of origin. These include facilities in India, Mexico, South Africa, Thailand, and Vietnam.³²³ The total mass of irradiated food products imported by country is found in Table 5.4: Mass (Kg) of Irradiated Products Entering the United States from Overseas below. Mexican produce may be treated in Mexico or upon arrival in the United States under the USDA Port of Entry program.³²⁴ Three commercial facilities in the United States have been certified for phytosanitary irradiation of imports under this relatively new program.

Table 5.4: Mass (Kg) of Irradiated Products Entering the United States from Overseas

Year	India	Mexico	South Africa	Thailand	Vietnam	Total
2007	0	0	0	195,000	0	195,000
2008	276,000	262,000	0	2,440,000	121,000	3,099,000
2009	132,000	3,559,000	0	2,247,000	117,000	6,055,000
2010	94,000	5,672,000	0	1,540,000	754,000	8,060,000
2011	80,000	5,539,000	0	743,000	1,445,000	7,807,000
2012	217,500	8,349,000	16,500	937,500	1,764,500	11,286,500
2013	283,000	9,526,000	16,500	1,060,500	1,967,500	12,853,500
2014	265,500	10,119,500	0	843,000	2,293,000	13,617,500

However, as noted in relation to pathogen reduction treatments for food, the most prominent international standards limit the maximum energy for x-ray treatments to 5 MeV.

³²² Jeffers, Laura A., "Commodity Approval & Irradiation as a Phytosanitary Treatment," USDA-APHIS Presentation, Texas A&M E-Beam Workshop, (2017).

³²³ Ibid.

³²⁴ Hallman, Guy J. and Paisan Loaharanu, "Phytosanitary Irradiation – Development and Application," Journal of Radiation Physics and Chemistry, Radiat. Phys. Chem (2016), <http://dx.doi.org/10.1016/j.radphyschem.2016.08.003>. Hallman, Guy J., Yves M. Hénon, Andrew G. Parker, and Carl M. Blackburn, "Phytosanitary irradiation: An overview," 2016 — Florida Entomologist — Volume 99, Special Issue 2 (2016).

Technical Requirements

Current FDA rules limit the maximum dose acceptable for preservation and disinfestation of fresh produce to 1,000 Gy.³²⁵ This upward limit poses a challenge at some facilities for the application of the minimum 400 Gy generic dose to standard sized processing volumes. Multi-purpose irradiation facilities not designed for the relatively low dose irradiation required for PI may have DURs as high as 3:1.³²⁶ A high DUR can be a challenge for PI because application of the minimum radiation dose (such as 400 Gy in the case of the generic standard) may result in a maximum dose above the FDA-allowable 1,000 Gy, depending on the size and density of the processed volume.³²⁷

No matter the type of radiation technology employed, the dose delivered throughout the target will vary, generally decreasing as the radiation penetrates further into the packaged product. The rate and extent of dose attenuation depends on the density of the packaged commodity. In a mixed-fruit box, for example, the different fruits might vary in size, shape, water content, and density; thus, the pattern of radiation dosing may be more variable compared with treatment of a more uniform box of one type of fruit.³²⁸

Follett and Weinert (2009) tested dose variation in boxes of single and mixed tropical fruits.³²⁹ The observed DUR ranged from a low of 1.3 for papaya alone to 1.37 for a mixture of papaya, longan, and banana. In all test cases, the treatments met the technical requirement of a 400-Gy minimum absorbed dose without exceeding the 1,000-Gy maximum allowable dose. The results showed that dose variation between fruit mixtures and single fruits is quite similar; therefore, radiation treatment of loads of mixed fruit using generic doses is technically feasible.

³²⁵ S. Pillai and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," in *Global Safety of Fresh Produce – A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014) 9.

³²⁶ Follett, Peter, "Phytosanitary Irradiation for Fresh Horticultural Commodities: Generic Treatments, Current Issues, and Next Steps," *Stewart Postharvest Review* (2014).

³²⁷ Ibid.

³²⁸ Barkai-Golan, Rivka and Peter A. Follett, *Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce*, Academic Press/Elsevier (2017).

³²⁹ Ibid.

Dose distributions will vary depending upon the radiation source, the technology and processing configuration, and the physical characteristics of the target. To ensure the effectiveness of a phytosanitary irradiation treatment, the entirety of the packaged product must receive at least the minimum dose required. However, this results in higher doses delivered to the areas of the target, closer to the edges of the package, which may diminish the quality of those portions of the product. The ability to tolerate radiation at higher doses varies among products.³³⁰

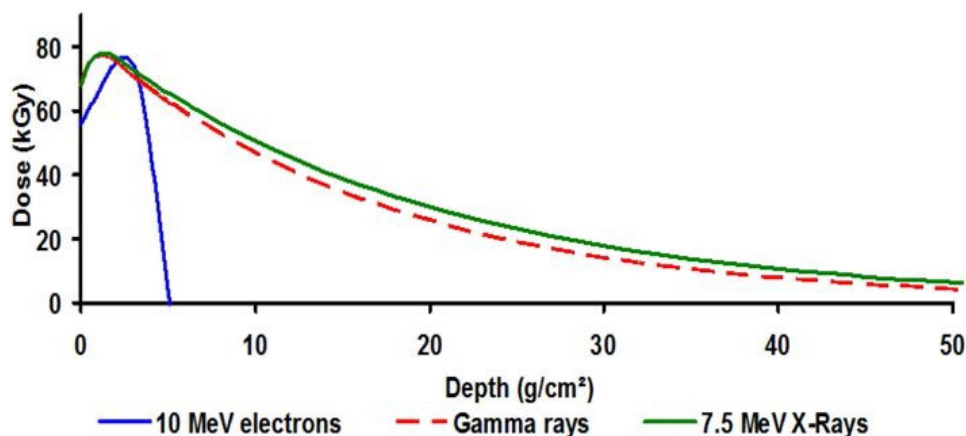


Figure 5.2: Compared Penetration of Ionizing Radiation International Atomic Energy Agency, “Manual of Good Practice in Food Irradiation,” Technical Reports Series No. 481 (2015).

In contrast to gamma and x-rays, accelerated electrons have a limited ability to penetrate targeted materials. As a result, there are limitations on the size of the packages or pallets that can be processed while still achieving the DUR necessary for phytosanitary irradiation. E-beam facilities used for these treatments typically process 5-pound packages compared with the larger pallets that may be used at x-ray or gamma facilities.³³¹ They also irradiate the product from two opposite sides. While technology considerations typically assume that transport and processing will rely on the larger pallets, the increasing quantity of fresh fruits and produce prepared and sold in either single or small serving sizes may challenge this assumption. If so, the reduced penetration capabilities of e-beams may be less of a disadvantage.”³³²

In addition, a relaxation in the dose limits required for product processing could enable e-beam processing volumes more often comparable to gamma and x-ray. This could be accomplished through a reduction in the minimum dose requirements for products and pests when consistent with effective treatment, or an increase in the maximum dose when consistent with safety and product quality.³³³ For example, there is evidence that the current generic 400 Gy dose accepted by the USDA (but not yet accepted internationally) could be reduced to 300 Gy.³³⁴ Similarly, 250 Gy has been accepted in New Zealand against a broad assortment of insects for which the USDA requires the 400 Gy generic minimum.³³⁵ In addition, research has

³³⁰ Hallman, Guy J., “Phytosanitary Applications of Irradiation,” *Comprehensive Reviews in Food Science and Food Safety*, Vol.10 (2011).

³³¹ Hallman, Guy J. and Carl M. Blackburn, “Phytosanitary Irradiation,” *Foods*, 2016, 5, 8; doi:10.3390/foods5010008.

³³² Pillai, S. and C. Bogran, “Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety,” in *Global Safety of Fresh Produce – A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014), page 231.

³³³ Hallman, Guy J., “Process Control in Phytosanitary Irradiation of Fresh Fruits and Vegetables as a Model for Other Phytosanitary Treatment Processes,” *Food Control* (2016).

³³⁴ Ibid.

³³⁵ Hallman, Guy J. and Paisan Loaharanu, “Phytosanitary Irradiation – Development and Application,” *Journal of Radiation Physics and Chemistry, Radiat. Phys. Chem* (2016), <http://dx.doi.org/10.1016/j.radphyschem.2016.08.003>.

shown that an increase in the maximum allowed dose from 1000 Gy to 2000 Gy would have no impact on the quality of treated products.³³⁶

To compensate for the more limited penetrating capability of e-beam radiation, e-beam facilities that offer phytosanitary irradiation services use smaller containers of packaged product for processing, with doses delivered from two or more sides. The processing volume may vary depending on factors including product density and accelerator energy, which can potentially be modulated or pulsed during processing to further improve the resulting DUR.³³⁷ For example, one manufacturer estimates that using 4 sided DUR with intensity modulation (ranging between 5 MeV and 10 MeV) a DUR of approximately 1.22 is possible.³³⁸

Lifecycle Technology Costs

Capital Requirements

The cost to establish an e-beam facility for phytosanitary irradiation purposes was estimated in 2014 to be between \$6 and \$8 million.³³⁹ However, these costs are quickly declining; current systems are estimated to cost between \$3 and \$4 million to establish.³⁴⁰ The layout of an e-beam facility generally depends on whether it is a multipurpose facility treating a range of food and non-food products or a specialty facility focused on phytosanitary irradiation. Other common design factors include the number of accelerators used in the treatment process and whether the facility also offers x-ray irradiation services.

Commercial e-beam facilities utilize accelerator power in the range of 12 kW to 20 kW. However, because the financial viability of a commercial irradiation facility depends largely on product throughput, accelerators in the range of 15 kW to 80 kW are now commercially available.³⁴¹ The key features in the design of e-beam treatment facilities include the types of products to be treated, the doses to be delivered, the preferred throughputs, and the capital costs of the equipment and the product handling systems.

These cost advantages, however, do not apply relative to e-beam technologies, primarily due to the electricity conversion inefficiencies. Technology and design improvements that make the conversion of e-beam to x-rays more efficient could improve the commercial feasibility x-ray for phytosanitary treatments.³⁴² There is currently only one commercial x-ray facility in the United States approved by the USDA for phytosanitary applications. In operation since 2000, the Hawaiian facility uses a 5 MeV x-ray to treat products destined for both the United States mainland and markets abroad.

Processing Cost Estimates

An advantage of e-beam irradiation relative to x-ray processing is the higher rate of electricity to radiation conversion. An additional benefit of e-beam relative to both x-ray and gamma radiation is that the required dose can be achieved very rapidly, potentially compensating for the reduced size of the processing pallets. E-

³³⁶ Brown, David, "The Truth About Radiation Processing: 'Niche Markets... Hidden Gems'" Mevex Corporation, presented at the 2017 Texas A&M Electron Beam Workshop

³³⁷ Ibid.

³³⁸ Ibid.

³³⁹ Pillai, S. and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," in *Global Safety of Fresh Produce – A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014).

³⁴⁰ Pillai, S. comments to the Working Group, May 2017.

³⁴¹ Pillai, S. and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," in *Global Safety of Fresh Produce – A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014).

³⁴² Ibid.

beam dose delivery times depend on the energy level of the electron generator, although e-beam energies greater than 10 MeV are prohibited for food and food-related products.³⁴³ Nevertheless, typical e-beam dose rates for PI treatments are roughly 3,700 Gy per second, substantially exceeding those provided by both x-ray and gamma sources.³⁴⁴

A key factor for the economic viability of an irradiation facility is sufficient volume to amortize the substantial initial capital costs.³⁴⁵ The capital cost to develop a gamma facility for phytosanitary applications is estimated to be significantly greater than the cost to develop an e-beam facility.³⁴⁶ A second key factor is the marginal processing cost of the product mix treated at the facility. By one assessment, costs for irradiation processing range from about \$0.10 per kg for fruits to approximately \$0.20 per kg for frozen ground beef. However, the same assessment notes that few business models have been developed to fully assess different irradiation technologies as applied to different sizes or types of producers, distributors, and retailers.³⁴⁷

Current efforts to reduce the generic minimum dose from 400 Gy to 300 Gy, as well as those tied to specific pests, could make irradiation technologies faster and therefore more cost effective.³⁴⁸ For example, the dose to control three quarantine pests in sweet potatoes was reduced from 400 Gy to 150 Gy; the change resulted in a 60 percent reduction in the cost of treatment.³⁴⁹ In addition, products that do not tolerate irradiation well at higher doses might become better candidates for irradiation treatment under reduced minimum doses. Similarly, an increase or elimination of the 1,000 Gy maximum dose for PI could increase the range of products treatable at multipurpose service centers with higher-energy devices.³⁵⁰

Cobalt-60 Supply and Price Constraints

Phytosanitary treatment facilities that use gamma sources depend on a steady supply of encapsulated cobalt-60 to regularly replace decayed sources. However, the worldwide supply of cobalt-60 is subject to current and potential supply constraints that may impact the operational cost of panoramic irradiation relative to alternatives.³⁵¹

There are currently two types of operational power reactor commonly used to produce cobalt-60. The first is a Canadian design, known as a CANDU reactor, and the other is a Russian design known as the RBMK.

³⁴³ Pillai, S. and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," in *Global Safety of Fresh Produce – A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014).

³⁴⁴ Pillai, S., "Principles of Ionizing Radiation and eBeam and X-ray Dose Deposition," Texas A&M University 2017.

³⁴⁵ Follett, P.A. and E.D. Weinert, "Phytosanitary irradiation of fresh tropical commodities in Hawaii: Generic treatments, commercial adoption, and current issues," *Radiation Physics and Chemistry* 81 (2012) 1064–1067.

³⁴⁶ Pillai, S. and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," in *Global Safety of Fresh Produce – A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014); Guy J. Hallman, "Process Control in Phytosanitary Irradiation of Fresh Fruits and Vegetables as a Model for Other Phytosanitary Treatment Processes," *Food Control* (2016), page 374.

³⁴⁷ Pillai, S. and C. Bogran, "Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety," in *Global Safety of Fresh Produce – A Handbook of Best Practice: Innovative Commercial Solutions and Case Studies*, Woodhead Publishing (2014), page 230.

³⁴⁸ Barkai-Golan, Rivka and Peter A. Follett, *Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce*, Academic Press/Elsevier (2017).

³⁴⁹ Follett, Peter, "Phytosanitary Irradiation for Fresh Horticultural Commodities: Generic Treatments, Current Issues, and Next Steps," *Stewart Postharvest Review* 2014, 3:1.

³⁵⁰ Follett, P. A. and Wall, Marisa M., "Phytosanitary irradiation for export of fresh produce: Commercial adoption in Hawaii and current issues," Publications from USDA-ARS/UNL Faculty, Paper 1416 (2012).

³⁵¹ Working Group member comments. See also, *Federal Trade Commission vs. Steris Corporation, et al.*, Plaintiff Federal Trade Commission's Complaint for Temporary Restraining Order and Preliminary Injunction, United States District Court Northern District Of Ohio Eastern Division, Case No. 1:15 CV 1080, June 4, 2015, page 5: "Some customers are concerned about the availability and pricing of gamma sterilization in the future due to questions about the supply of Cobalt 60. As a result, e-beam may become a closer economic substitute for gamma than it is today."

There are 18 CANDU reactors located in Ontario, Canada, of which only 7 are currently producing cobalt-60. Additionally, there are CANDU reactors in China, Argentina, Romania, South Korea and India, some of which currently produce cobalt-60. There are 11 RBMK reactors in Russia, only 7 of which are currently producing cobalt-60. Cobalt-60 is also produced in research reactors such as the 3 reactors at Mayak and Dmitrovgrad Russia. The typical irradiation time to produce cobalt-60 is about 18 months to three years in CANDU reactors and up to five years in the RBMK reactors.³⁵²

However, in the next 5 to 10 years, a significant number of these reactors are scheduled to cease operations or undergo maintenance outages. In Canada, the Ontario Power Generation (OPG) reactors, are scheduled to permanently cease operations in 2024.³⁵³ In addition, the other four cobalt-60 production reactors in Canada are scheduled for a refurbishment process that will extend the life, and cobalt production capability of these reactors to 2064. During the refurbishment, one reactor at a time will be taken off-line, reducing the amount of cobalt produced during this 10-year period. Over the next 15 years Russia will phase out its RBMK reactors and replace them with newer “VVER” designs which have the potential to produce cobalt-60.³⁵⁴

Nordion, among others, is taking steps to increase the global supply of cobalt-60 by:

- Extending contracts with reactors currently producing cobalt
- Working with the owners of the other CANDU reactors currently not producing cobalt
- Bringing more RBMK reactors into cobalt-60 production
- Acquiring and deploying technology to produce cobalt in light water reactors (of which there are more than 90 operational in the United States and more than 350 globally)

In February 2019, the company stated that the “technology’s viability has already been demonstrated in a pilot program that successfully produced approximately one million [c]uries of Cobalt-60 at two United States reactors.”³⁵⁵ The company has not yet provided a timeline or supply estimates for expanded production using the new technology.

Device Ability to Meet Site and Application Requirements

The following factors largely govern the selection of irradiator design:³⁵⁶

- **Means of transporting food products:** The mechanical design of the irradiation and transport systems, including the source-to-product geometry in a given process, as required by the form of the product, e.g., bulk or packaged, and its properties.
- **Range of doses:** The range of doses needed to process a wide variety of products for various applications.
- **Throughput:** The amount of product to be processed within a defined period of time.
- **Reliability:** The property of providing correct performance as needed.

³⁵² World Nuclear Association, “Radioisotopes in Medicine,” accessed January 2019, <http://www.world-nuclear.org/information-library/non-power-nuclear-applications/radioisotopes-research/radioisotopes-in-medicine.aspx>.

³⁵³ Ontario Energy Board, Province of Ontario, Canada, “Ontario’s Long Term Energy Plan 2017: Delivering Fairness and Choice,” <https://www.ontario.ca/document/2017-long-term-energy-plan>.

³⁵⁴ World Nuclear Association, “Radioisotopes in Medicine,” accessed January 2019, <http://www.world-nuclear.org/information-library/non-power-nuclear-applications/radioisotopes-research/radioisotopes-in-medicine.aspx>.

³⁵⁵ Sotera Health, “Nordion Acquires Technology to Expand Future Global Cobalt-60 Supply,” last visited August 6, 2019, <https://www.nordion.com/nordion-acquires-technology-to-expand-future-global-cobalt-60-supply/>.

³⁵⁶ Codex Alimentarius, Code of Practice for Radiation Processing of Food (CAC/RCP 19-1979).

- **Safety-systems:** The systems intended to protect operating personnel from hazards posed by radiation.
- **Compliance:** The adherence to good manufacturing practices and relevant government regulations. **Capital and operational costs:** The basic economic considerations necessary for sustainable operation.

Administrative and Regulatory Costs

Safety and Security Controls

Currently operational industrial scale gamma irradiator facilities are designed to meet standards developed by the IAEA and ANSI/HPS, and must meet United States NRC design requirements under 10 C.F.R. Part 36, “Licenses and Radiation Safety Requirements for Irradiators.” The physical security of industrial gamma irradiators is also regulated and the requirements of under 10 C.F.R. Part 37 “Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material,”³⁵⁷ apply, including requirements for background investigations; access controls; security plans; immediate detection, assessment, and response to unauthorized access; tracking of shipments; security barriers; and other requirements. Security measures are incorporated into all aspects of the industry including the design of the irradiators, the transportation of the sources, and the design, construction, operation and maintenance of the facilities. The NRC estimated an initial cost of approximately \$21,736 to maintain the Part 37 security requirements.³⁵⁸

All shipping containers used to transport Cobalt-60 in the United States must meet U.S. Department of Transportation (DOT) and NRC safety requirements. Sources transported to and from industrial irradiation facilities during reloading are shipped in large “Type B” transport casks designed according to stringent safety and security standards. A typical cobalt-60 finished source transport container, licensed to carry about 200,000 Ci of Cobalt-60, is approximately 1.5-m tall by 1.2-m diameter (5-ft tall by 4-ft diameter) and weighs many tons.

Disposal Costs and Considerations

The large cobalt-60 sources used in the industrial scale irradiation facilities most commonly used for food treatment applications are typically used for 20 years from the date of purchase, although some facilities will keep sources longer if they have sufficient irradiator rack space. Most cobalt-60 manufacturers will accept return of sources under separately negotiated contracts. Disused cobalt-60 sources remain highly radioactive and are handled and transported in the same manner as new cobalt-60 sources.

When return to the manufacturer is not possible, the source licensee is responsible for the safe and secure long-term management of these sources pending disposal. In such cases, the facility typically treats the used cobalt-60 in much the same way as spent nuclear fuel, storing the material under water until it has decayed to the point that it can be placed into dry storage containers within the facility perimeter. Cobalt-60 industrial irradiator sources are double-encapsulated in welded stainless steel that does not dissolve in water, enabling safe storage in a water pool for decades. Companies operating commercial gamma irradiators are required to provide a financial guarantee to the State (Agreement States) or Federal Government (NRC) for the costs of decommissioning the irradiator operator’s facility, and disposition of the sources in it.

³⁵⁷ Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material, 10 C.F.R. § 37.

³⁵⁸ Ibid.

Currently, return to manufacturer arrangements are available for most phytosanitary and food facilities. The source manufacturer typically recycles the decayed material by combining it with newly manufactured, very high activity cobalt-60 to create a new industrial irradiator source. For example, Nordion has recycled almost 20,000 cobalt-60 sources with a combined activity of almost 9 million Ci since it initiated recycling in 2003. The company expects to recycle thousands of additional sources with a combined activity of millions of Ci over the next several years. In addition to manufacturer recycling, a much smaller number of sources are purchased by specialty companies and re-encapsulated for use in other devices.

In general, as commercial sealed source disposal access becomes available, the commercial licensees who benefit financially from the use of the material are responsible for the disposition costs related to their disused sources. In the past, commercial disposal access challenges and security concerns related to high-activity sources has led on certain occasions to a temporary increase in government involvement, including the assumption of significant costs related to the disposal of sealed sources used in phytosanitary and food irradiators. However, the 2015 revised Concentration Averaging Branch Technical Position reinforced that currently operational “near-surface” disposal facilities can accept even the highest activity cobalt-60 sources as Class B waste.

Chapter 6: Alternative Technologies for Sterile Insect Technique

Introduction

The sterile insect technique (SIT), or sterile insect release method (SIRM), is a type of pest control used to suppress or eradicate a pest species in a given area. SIT involves the use of ionizing radiation, typically from self-shielded or panoramic irradiators that use cesium-137 or cobalt-60 gamma radiation sources, to reproductively sterilize insects or their larvae in a laboratory environment. The sterilized insects are then released into the targeted environment in order to mate with the indigenous non-sterilized insect population. No offspring are produced as an outcome of this coupling, resulting in a reduction of the pest population. The consistent introduction of sterile insects over many reproductive cycles can result in either the functional eradication of a pest species in the targeted area, or the control of a pest population sufficiently to reduce its negative societal impacts (e.g., crop damage, disease) to a tolerable level.

The ionizing radiation from x-ray or e-beam devices is the most likely replacement option for SIT applications. As a result, this chapter will consider the potential viability of these technologies. There are other types of pest control methods which can complement SIT; however, these methods are not viable as replacements for radiation, and therefore not considered further in this paper.

Sterile Insect Technique Overview

SIT has been an effective method of pest control since the 1960s. It has been used to control or eradicate several important pests, including fruit flies, moths, screwworms, and tsetse flies. The technique is currently applied on six continents as a component of area-wide integrated pest management (AW-IPM) programs for insect pest control.³⁵⁹ There is also increasing interest in using the method to help control the spread of mosquito-borne diseases.³⁶⁰

SIT uses ionizing radiation—usually gamma rays, though x-rays and e-beams may also be used—to induce sterility in insect larvae, pupae, or adults. The radiation breaks the molecular bonds in the insect DNA in the sperm, which leads to sterility. The radiobiological effectiveness of gamma rays, x-rays, and e-beams are generally considered to be equivalent for SIT applications.³⁶¹ However, this same radiation may induce damage in other cells in an insect and can reduce its quality or ability to survive and function in the wild. Insect response to radiation varies by species and life stage within a species. As a result, it is necessary to determine the dose response curves for each target species.³⁶²

There is also a natural trade-off between sterility level and performance. The optimal dose should be selected to produce the highest sterility level without compromising the performance, or survivability, of the

³⁵⁹ Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, “Sterile Insect Technique,” accessed October 3, 2018, <http://www-naweb.iaea.org/nafa/ipc/sterile-insect-technique.html>.

³⁶⁰ International Atomic Energy Agency, “Thematic Plan for the Development and Application of the Sterile Insect Technique (SIT) and Related Genetic and Biological Control Methods for Disease Transmitting Mosquitoes,” IAEA TC project INT0089 - Developing Human Resources and Supporting Nuclear Technology (2014).

³⁶¹ Bakri, A., K. Mehta and D. R. Lance, “Sterilizing Insects with Ionizing Radiation” V. A. Dyck, J. Hendrichs, and A.S. Robinson, Eds., *Sterile Insect Technique: Principles and Practice in Area-Wide Integrated Pest Management*, IAEA; Springer (2005), 236.

³⁶² Ibid.

sterile insects, and thus the highest capacity to induce sterility in the local population.³⁶³ This survival period includes the laboratory to the target area and the ability to survive predators and natural conditions in the wild. The sterilized insect should be healthy enough to find and copulate with a non-sterilized insect. If the dose is too low, a partially fertile insect would be released, reducing the impact of the SIT. Therefore, the dose to the insect must fall in a specific range.³⁶⁴ The dose-response curves are now well-developed for many important species.³⁶⁵

The IPPC states that SIT differs from classic biological controls in that sterile insects are not self-replicating and therefore cannot become established in the environment. SIT is further different from classical biological control because it is species-specific and does not introduce non-native species into an ecosystem.³⁶⁶

Wild pest insect populations can reach thousands per hectare, and most insect pests create several generations per year. Because they cover large geographic areas, if the reproductive rate of a population is reduced or eliminated in one area, that area could be repopulated by neighboring insects of the same species in a relatively short period of time. Therefore, to be an effective pest control option, SIT must release a considerable number of sterile insects into an environment at regular intervals on an areawide basis.³⁶⁷ The number of sterilized insects required will vary based on the species and region, but the total is between millions and billions of sterilized insects per week.³⁶⁸ There are numerous SIT facilities with large capacities spread around the world—currently 66 facilities in 39 countries—in part to reduce transit time from irradiation to dispersal site.

Worldwide, the potential exists to produce and irradiate more than 6.7 billion insects per week, but in practice the actual number is less.³⁶⁹ Most SIT irradiations are conducted for fruit fly species, but large irradiation programs also exist for screwworms and moths as well as to irradiate insect eggs, larvae, or pupae to enhance the production of parasitoids.³⁷⁰ Smaller research and development programs exist for mosquitos and tsetse flies, and SIT is frequently combined with other pest control techniques to maximize the ability of all methods to control or eradicate the pest population. The combination and distribution of pest control technique will vary based on species and region of interest.

The major challenges in developing optimal mass-rearing procedures include delivering a uniform radiation dose, separating males and females, and minimizing the impact of handling and irradiation. Success is measured by the number, quality, and competitiveness of the resulting adult insects as well as the complete

³⁶³ Parker, A. and K. Mehta, “Sterile insect technique: a model for dose optimization for improved sterile insect quality,” *Florida Entomologist* 90 (2007) 88–95.

³⁶⁴ Ibid.

³⁶⁵ International Atomic Energy Agency (IAEA), “International Database on Insect Disinfestation and Sterilization (IDIDAS),” Accessed November 27, 2018. [https://nucleus.iaea.org/sites/naipc/ididas/SitePages/International%20Database%20on%20Insect%20Disinfestation%20and%20Sterilization%20\(IDIDAS\).aspx](https://nucleus.iaea.org/sites/naipc/ididas/SitePages/International%20Database%20on%20Insect%20Disinfestation%20and%20Sterilization%20(IDIDAS).aspx).

³⁶⁶ International Plant Protection Convention (IPPC), “International standards for phytosanitary measures,” Food and Agriculture Organization of the United Nations, ISSN 2521-7232.

³⁶⁷ Klassen, W., “Area-wide integrated pest management and the sterile insect technique,” in V. A. Dyck, J. Hendrichs, and A.S. Robinson, Eds., *Sterile Insect Technique: Principles and Practice in Area-Wide Integrated Pest Management*, IAEA; Springer (2005) 39.

³⁶⁸ Enkerlin, W. R., A. Bakri, C. Caceres, J. P. Cayol, A. Dyck, U. Feldmann, et al. “Insect pest intervention using the sterile insect technique: Current status on research and on operational programs in the world,” Research Institute for Subtropics, Naha; Japan (2003) 11–24.

³⁶⁹ Parker, Andrew, “Sterile Insect Technique: Irradiators for SIT,” for the Nuclear Alternate Technologies Working Group, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, September 12, 2018.

³⁷⁰ Cancino, Jorge, Lía Ruíz, Mariana Viscarret, John Sivinski and Jorge Hendrichs, “Application of Nuclear Techniques to Improve the Mass Production and Management of Fruit Fly Parasitoids,” *Insects* 3 (2012) 1105–1125, doi:10.3390/insects3041105; Sarwar, M., N. Ahmad, A. Rashid, and S. M. M. Shah, “Valuation of gamma irradiation for proficient production of parasitoids (Hymenoptera: Chalcididae & Eucilidae) in the management of the peach fruit-fly, *Bactrocera zonata* (Saunders),” *International Journal of Pest Management* 61 (2015) 126–134; Cancino, J., L. Ruiz, J. Perez, and E. Harris, “Irradiation of *Anastrepha ludens* (Diptera: Tephritidae) eggs for the rearing of the fruit fly parasitoids, *Fopius arisanus* and *Diachasmimorpha longicaudata* (Hymenoptera: Braconidae),” *Biocontrol Science and Technology* 19 (2009) S1, 167–177.

suppression of fertile insect emergence in the wild. It is generally more effective to release only sterile males to prevent the sterile males wasting time courting and mating with sterile females. This technique is also effective because, even when sterile, female fruit flies may still damage fruit when they pierce the skin in attempting to lay eggs and female mosquitoes may still transmit disease when they feed on blood. To be most effective, the released sterilized males should substantially outnumber the native non-sterilized males to increase the odds of a non-viable pairing.³⁷¹

The process for separating males from females prior to irradiation is labor intensive, especially since the number of insects that require separation can be in the hundreds of millions per week. Sexing strains based on pupal color³⁷² or a temperature-sensitive lethal trait³⁷³ have been developed for some insect species; for others, however, the sorting can be a limiting factor in production and in many cases is not practical (e.g., New World screwworm).

In production laboratories, non-sterilized females are kept and bred with non-sterilized males to produce additional stock for release into the environment. Laboratory-bred insects are not subject to non-cannibalistic predation or other natural population controls and would reproduce exponentially subject to food availability.

The dose rate in any practical irradiator varies within the irradiation volume. It is common to define the minimum dose (the dose received at the lowest-dose rate point in the irradiation volume), which means that other insects will receive higher doses in the higher-dose rate points. It is important, therefore, to arrange the load of insects within the irradiation volume to minimize the DUR to ensure the insects at the higher-dose rate points are not significantly impaired by the higher dose. A DUR of less than 1.3 is generally considered acceptable.³⁷⁴

The ISO standard for SIT can be found in ISO / ASTM51940.

Commercially Available Sterile Insect Technique Technology – Isotopic and Alternatives

Gamma Irradiation

SIT is typically conducted with small gamma irradiator units using cobalt-60 or cesium-137. Presently, there are 24 self-contained cobalt-60 units, 18 panoramic cobalt-60 units and 10 cesium-137 units in use for SIT worldwide. Cobalt-60 is a beta and gamma ray emitting radioisotope with a 5.27-year half-life. The average gamma energy of cobalt-60 is 1.25 MeV. Cesium-137 is also a beta and gamma emitter, but it has a 30-year half-life.

Panoramic facilities currently have the highest capacity of all SIT devices. They can irradiate large volumes, but in a typical commercial irradiation plant the DUR can be greater than 2. It is possible to reduce the DUR, but this comes at the expense of loading efficiency. Achieving appropriate doses in commercial irradiators can be difficult as most are designed to apply doses of tens of thousands of gray over a period of several

³⁷¹ Barclay, Hugh John, "Determination of the sterile release rate for stopping growing age-structured populations," *International Journal of Pest Management* 62 (2015) 40–54.

³⁷² Busch-Petersen, E. and A. Kafu, "Assessment of quality control parameters during mass rearing of a pupal colour genetic sexing strain of the Mediterranean fruit fly," *Entomologia Experimentalis et Applicata* 51 (1989) 241–248.

³⁷³ Fisher, K., "Genetic sexing strains of Mediterranean fruit fly (Diptera: Tephritidae); Optimizing high temperature treatment of mass-reared temperature-sensitive lethal strains," *Journal of Economic Entomology* 91 (1998) 1406–1414.

³⁷⁴ Parker, Andrew, "Sterile Insect Technique: Irradiators for SIT," for the Nuclear Alternate Technologies Working Group, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, September 12, 2018.

hours for medical equipment sterilization or polymer modification. Panoramic irradiators, which are described in more detail in chapters 4 and 5, are the system of choice for large SIT projects, although no panoramic irradiators are currently in use in the United States for SIT.³⁷⁵

Self-contained cobalt-60 or cesium-137 units house up to 24,000 Ci of cobalt-60 or 12,000 Ci of cesium-137, which could produce about 200 or 40 Gy/min central dose rate, respectively. But they have limited throughput of insect irradiations and are typically for small to medium sized SIT programs, or for research and development. They have poor DUR, often in great excess of 2 so the usable volume for a DUR of 1.3 or less is further restricted. Self-contained units incorporate permanent lead shielding and do not require additional shielding but weigh from 5-7 tons and require access control for security. Samples for irradiation are placed in the chamber which travels to the irradiate position and returns to the load position after a set time. Doses are much higher than typical in panoramic irradiators, so exposure times are correspondingly short (a few minutes). Five programs in the United States currently utilize self-contained irradiators, four cesium-137 and one cobalt-60.

X-ray Irradiation

The primary non-isotopic alternative for SIT is the use of low-energy x-rays (150 to 225 keV) to induce sterility. X-ray devices generate a spectrum of energies, from the peak energy down to zero,³⁷⁶ with the average energy at roughly one third of the maximum energy, whereas gamma units produce photons in distinct and well-known specific energies.

X-ray units operate on demand, at lower energies, and can be turned off and on. This is beneficial from a safety perspective (due to reduced shielding requirements) and a security perspective, but it also requires a steady, reliable, and large power source to operate. X-ray irradiator units tend to have lower insect throughputs than isotope-based SIT units because of the lower dose and penetration of the radiation. They can have decent DUR with appropriate filtration,³⁷⁷ but this reduces the dose rate and resulting throughput.³⁷⁸

A key challenge—and an area of active research—is lowering the DUR for low energy x-ray machines. For instance, there are some areas for improvement involving the orientation of the x-ray beams and the positioning and movement of the samples. It is preferable to have a horizontal x-ray beam because it can apply a more uniform dose to a cylindrical source when the cylinder is rotated about a vertical axis. Vertical axis rotation is easier to achieve in practice than horizontal axis rotation, and for irradiation of samples in water (e.g., mosquito pupae) vertical axis rotation reduces the risk of water spillage in the irradiator if a canister lid is not correctly fitted. The DUR can also be improved by flipping or rotating the target medium during irradiation.

Worldwide there are currently nine x-rays units performing SIT, with another five units planned or under construction (one planned unit in Africa will directly replace a cesium-137 unit). There is one x-ray system in the United States: The Light Brown Apple Moth Unit in California. X-ray units are smaller than the self-contained gamma irradiators, typically weighing approximately 1 ton and require no special housing

³⁷⁵ Parker, Andrew, “Sterile Insect Technique: Irradiators for SIT,” for the Nuclear Alternate Technologies Working Group, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, September 12, 2018.

³⁷⁶ Mehta, K. and A. Parker, “Characterization and dosimetry of a practical x-ray alternative to self-shielded gamma irradiators,” *Radiation Physics and Chemistry*, 80 (2011) 107–113.

³⁷⁷ Parker, Andrew, “Sterile Insect Technique: Irradiators for SIT,” for the Nuclear Alternate Technologies Working Group, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, September 12, 2018.

³⁷⁸ Filtration consists of adding additional material between the ionizing photon source and the target material. This filtration attenuates the low-energy photons and reduces the surface dose deposition into the target material. This has the effect of improving the DUR of the irradiation process.

facilities. But whereas isotopic irradiators can be calibrated using standard transfer dosimeters from an accredited laboratory, the wide spectrum and low energy of photons from x-ray units makes calibration more difficult, as most standard dosimetry systems are not calibrated at these low energies.

E-beam Irradiation

E-beam machines produce high-intensity focused beams of high-energy (1 to 10 MeV) electrons and can be either continuous or pulsed beam. Pulsing allows the average beam power to be adjusted by changing the pulse length, and the beam can be scanned across a conveyor to irradiate samples passing underneath. The very high dose rates of most e-beam systems make them unsuitable for direct application for SIT. However, the high-energy e-beam can be converted to x-rays by introducing a high-atomic-number material target into the beam. Even accounting for the low conversion efficiency to photons, the dose rates are still very high, requiring very short pulses and high conveyor speeds to achieve low enough doses for SIT.

There is currently only one e-beam facility conducting SIT irradiations: a commercial provider in Europe performing irradiations on pupae of the fruit fly *C. capitata*.³⁷⁹ As such, there is currently little practical experience with e-beam SIT technology. However, it has significant potential as an alternative technology. It does not use any radioisotopes and thus has few radiological security concerns; in addition, it is an on-demand technology and therefore can be turned off and on at will, which has benefits with regards to worker safety, although shielding requirements may be high.

E-beam can have high to very high relative insect throughput, with decent penetration depth for SIT. Like all radiation-based SIT technologies, e-beam has DUR challenges. For instance, dose distribution can be difficult to control if the pulse length must be set very short to achieve a low enough dose.³⁸⁰ Also, the technology is currently expensive for SIT applications, in part due to the lack of available options. It will require a reliable high energy power source and the necessary expertise to operate.

Other Insect Sterilization Techniques

Although chemical sterilants have been tested as alternatives and used on occasion, ionizing radiation is generally accepted as the most effective method for insect sterilization.³⁸¹ Chemical sterilants pose significant environmental and occupational hazards and treated insect species could potentially develop a resistance to their sterilizing effects. In contrast, the precise damage to the reproductive capabilities of insects treated with ionizing radiation is sufficiently random to make the development of resistance impossible.³⁸²

There are other techniques for sterilizing insects in a lab and then releasing them into the wild that do not use radiation; these include incompatible insect technique and genetic modification. Neither of these techniques are considered SIT in the traditional sense but could be used as complimentary or alternate forms of pest control. As noted earlier in this chapter, these techniques are outside the scope of this paper.

³⁷⁹ Parker, Andrew, "Sterile Insect Technique: Irradiators for SIT," for the Nuclear Alternate Technologies Working Group, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, September 12, 2018.

³⁸⁰ Ibid.

³⁸¹ Bakri, A., K. Mehta and D. R. Lance, "Sterilizing Insects with Ionizing Radiation" V. A. Dyck, J. Hendrichs, and A.S. Robinson, Eds., *Sterile Insect Technique: Principles and Practice in Area-Wide Integrated Pest Management*, IAEA; Springer (2005).

³⁸² International Atomic Energy Agency, "Thematic Plan for the Development and Application of the Sterile Insect Technique (SIT) and Related Genetic and Biological Control Methods for Disease Transmitting Mosquitoes," IAEA TC project INT0089 - Developing Human Resources and Supporting Nuclear Technology (2014).

Inherited Sterility

Some insect orders are more resistant to irradiation sterilization than others (e.g., Lepidoptera: moths and butterflies). In those orders, the radiation dose required to achieve sterility may be very close to the lethal dose, or the dose may be so high that the insect is seriously wounded and there is a reduced chance of finding a healthy reproductive partner upon release in the wild. However, radiation may still be used to reduce or eradicate those insects using a practice called inherited, or F1, sterility. In this method, males are subject to a sub-sterilizing dose of radiation and released to mate with wild females. The pairing will result in reduced progeny with a higher-than-normal proportion of F1 male offspring and near sterility in the male progeny; the few females are often completely sterile. The F1 males will continue to affect future reproduction in the population for several generations.

Similar to SIT, the F1 technique requires multiple iterations of irradiating insects in a controlled setting, then releasing them into the wild to reproduce with wild insects. SIT and F1 use similar irradiation equipment, although the target dose and throughput times are different. Therefore, the baseline gamma and x-ray technologies described in the sections above would apply equally to both SIT and F1 methods.

Technology Purchase and Replacement Considerations

The following section outlines considerations potential buyers would base their purchase/replacement decisions on, including device ability to meet site and application requirements, cost, and security factors of each technology.

Lifecycle Technology Costs

Chapter 4: Accelerator design improvements have increased the potential for both e-beam and x-ray to replace gamma for SIT applications, but the selection is based heavily on the devices' ability to meet strict DUR and time constraints. However, even by overall irradiation industry standards (both isotopic and alternatives), SIT is a niche market, and there is limited equipment built specifically for this purpose. A non-proprietary capital comparison of isotopic, e-beam, and x-ray facilities was not available at the time of this writing.

Device Ability to Meet Site and Application Requirements

Perhaps the most important factor in considering an alternative technology for SIT is its ability to deliver a narrow dose (not too high or low) of radiation in a short period of time to the target insects. The insects should also be kept in environmental conditions that would not otherwise harm them. Furthermore, the throughput of the SIT facility should be sufficiently large to produce enough sterilized insects such that their release can noticeably reduce the wild pest population. Lastly, the irradiations should occur near the target dispersion site, as transportation conditions and time can reduce the insects' survivability and ability to engage in reproductive acts once in the wild.

X-ray SIT units can provide the narrow dose range required for the insect species. The devices can feature advanced filtration designs for a desirable DUR. However, the lower throughput typically afforded by x-rays may increase the total irradiation time to sterilize the insects. This both reduces the facility throughput and limits the useful reproductive lifetime in the wild for the insects.

Administrative and Regulatory Costs

SIT-facility users must consider cost, researcher, and operational needs to maximize results. To transition to alternative technologies, users must understand what benefits these devices would offer and trust that they

would meet production requirements. A primary operational cost for gamma irradiators is the security required for the devices.

Safety and Security Controls

Currently operational industrial-scale gamma irradiator facilities are designed to meet standards developed by the IAEA and ANSI/HPS and must meet United States NRC design requirements under 10 C.F.R. Part 36, “Licenses and Radiation Safety Requirements for Irradiators.” The physical security of industrial gamma irradiators is subject to 10 C.F.R. Part 37 “Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material,” which includes requirements for background investigations; access controls; security plans; immediate detection, assessment, and response to unauthorized access; tracking of shipments; security barriers; and other requirements.³⁸³ Security measures are incorporated into all aspects of the industry, including the design of the irradiators, the transportation of the sources, and the design, construction, operation, and maintenance of the facilities. The NRC estimated an initial cost of approximately \$21,736 to maintain the Part 37 security requirements.³⁸⁴

Disposal Costs and Considerations for Sealed Sterile Insect Technique Devices

The proper disposal of radioactive materials used by the private sector is the responsibility of the licensees who benefit from them commercially. However, commercial disposal access challenges and security concerns related to high-activity sources has led to a temporary increase in government involvement, including the assumption of significant costs related to disposal.

Disposal and Constraints

Recently updated NRC disposal guidance likely enables radioactive material licensees to dispose of some high-activity cesium-137 sources (potentially up to the ~957 Ci Class C limit) and most or all cobalt-60 sources at currently operational commercial radioactive waste disposal facilities. Furthermore, DOE has made significant progress toward establishing a disposal pathway for certain risk-significant radioactive sources, such as the GTCC cesium-137 sources used in blood and research irradiators.³⁸⁵

Although the ultimate cost structure that will apply to GTCC sources remains uncertain, current commercial LLRW disposal costs are based on the volume and Ci of the waste (in addition to costs related to transportation). For example, using publicly available information, the cost to dispose of a single cesium-137 irradiator source at the only currently operational commercial disposal facility that allows nationwide access

³⁸³ Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material, 10 C.F.R. § 37.

³⁸⁴ U.S. Nuclear Regulatory Commission, “Rulemaking Issue Affirmation: Final Rule: Physical Protection of Byproduct Material, (10 C.F.R. Parts 20, 30, 32, 33, 34, 35, 36, 37, 39, 51, 71, and 73),” (Washington, DC: December 2011), available at <http://www.nrc.gov/reading-rm/doc-collections/commission/secys/2011/2011-0170scy.pdf>

³⁸⁵ In February 2016, DOE issued its “Final Environmental Impact Statement for the Disposal of Greater-Than-Class C (GTCC) Low-Level Radioactive Waste and GTCC-Like Waste,” and submitted the Report to Congress in 2017 describing the alternatives considered in the Final EIS and other related information, as required by Section 631 of the EPA Act. In an October 2018 Environmental Assessment, DOE “proposed to dispose of the entire GTCC LLW and GTCC-like waste inventory detailed in the Final EIS in the WCS [Federal Waste Facility] located in Andrews County, Texas,” a currently operational facility. A final Record of Decision remains pending. (See Department of Energy, “Environmental Assessment for the Disposal of Greater-Than-Class C (GTCC) Low-Level Radioactive Waste and GTCC-Like Waste at Waste Control Specialists, Andrews County, Texas,” Washington DC, October 2018.)

exceeds \$200,000.³⁸⁶ Packaging and transportation costs could add tens of thousands of dollars to the total cost.

Pending the availability of commercial disposal options, the NNSA/OSRP recovers and disposes of high-activity sources in the interest of National security, public health, and safety at federal facilities primarily intended for the disposal of waste generated by the United States government.³⁸⁷ Commercial radioactive material licensees may register their sources with NNSA/OSRP, which prioritizes them for recovery according to criteria determined in consultation with the NRC. Licensees are responsible for on-site security costs until their devices can be removed.

Furthermore, to help address a shortage of certified “Type B” transportation containers, NNSA has designed and certified two new Type B containers to transport common disused high-activity cesium-137 and cobalt-60 devices. These new packages will enable NNSA/OSRP to transport a majority of the high-activity cesium-137 and cobalt-60 devices and sources it is likely to encounter for the foreseeable future. Additionally, to encourage the development of commercially available containers, DOE/NNSA is facilitating the use of the NNSA container designs by commercial vendors.

Recycle

Some irradiator manufacturers will accept return of cobalt-60 of their own devices for source recycling. This reduces environmental and cost impacts of disposal, but usually at additional cost to the licensee.

³⁸⁶ Texas Administrative Code, Title 30, Part 1, Chapter 336, Texas Commission on Environmental Quality, Radioactive Substance Rules, Subchapter N, “Fees For Low-Level Radioactive Waste Disposal.”

³⁸⁷ These sites operate under different legislative authorities from those that govern the development or designation of a facility for disposal of commercially generated GTCC, and are prohibited from accepting waste, including sealed sources, directly from commercial radioactive waste generators.

Chapter 7: Alternative Technologies for Well Logging

Introduction

Well logging refers to the continuous characterization of geological formations surrounding a borehole (or well). Common well logging applications include fundamental earth science studies, aquifer identification, and environmental monitoring, including at radioactive waste burial sites. However, the most common and economically important well logging applications in the United States are in the exploration and development of petroleum and natural gas. These applications are the focus of this chapter.

Well logging tools include of the instruments that are used downhole to record data versus depth, as well as the associated techniques used by well loggers to interpret the logging data. Two modes of well logging are most commonly practiced: wireline logging involves lowering instruments into vertical holes post-drilling to acquire the geologic characterization data, whereas logging-while-drilling (LWD) uses instruments attached to the drilling assembly to perform geologic measurements as the drilling proceeds. LWD is used to interrogate difficult geological conditions or to reach reservoirs discovered during horizontal drilling (especially at offshore sites where drilling of numerous vertical wells is unfeasible).

Overview of Well Logging Science

There are several important parameters measured when well logging: density, porosity, lithology, mineralogy, and fluid saturation. The parameter values determined by logging data are often benchmarked against results from laboratory analysis of rock samples acquired downhole, at specific depths, using special coring techniques; continuous acquisition of rock samples would be unrealistic. Collectively, well logging measurements and the laboratory measurements of core samples are often denoted as petrophysical measurements.³⁸⁸

Many different technologies may be used to log a well (i.e., to characterize and quantify the surrounding geology). Presently, radioisotope-based technologies (such as gamma backscatter, neutron backscatter, and neutron capture spectra³⁸⁹) are the most common means of determining the density, porosity, lithology, and mineralogy of geologic formations, while electrical techniques are used to determine the fluid saturation. Finally, acoustic and NMR techniques can provide additional information, such as rock mechanical properties and fluid types, respectively, in addition to providing confirmatory measures of porosity.

Petrophysical measurements may be accompanied by downhole temperature and pressure measurements, especially to monitor the performance of producing cased wells.³⁹⁰ Well logging measurements generally determine near-bore formation properties (usually from inches to several feet) and often follow seismic

³⁸⁸ Ellis, Darwin V. and Julian M. Singer, *Well Logging for Earth Scientists*, Second Edition, Springer, New York, 2007.

³⁸⁹ Backscatter is the reflection of subatomic particles or photons at diffuse angles and reduced energies.

³⁹⁰ Cooke Jr., Claude E., "Radial Differential Temperature (RDT) Logging - A New Tool for Detecting and Treating Flow Behind Casing," SPE-7558-PA, *Journal of Petroleum Technology*, 1979, 31 (6): 676-682.

surveys that can measure formation properties across large extents, often in miles (see Acoustic Techniques below).

The porosity of the geological formation, often identified as the most important parameter to consider during exploration, is the fraction (by volume) of the rock that contains voids. The saturation of a given fluid in the formation is the fraction of the pore volume filled by the fluid (e.g., water, oil, or gas). The density-based porosity is the most accurate downhole measure of porosity. Porosity and saturation together determine the reserves volume in oil/gas exploration. Furthermore, since small errors in porosity can have a large impact on well-reserve estimates, an accurate measure of porosity is essential: It should be within one “porosity unit” (pu)³⁹¹ to provide a reliable estimate of the reservoir size for economic decision-making purposes. The actual effect of porosity error on the reserve estimate depends on the nominal porosity of an individual formation and its nominal reservoir size. For example, 1-pu uncertainty in a 15-pu formation with a 10-billion-barrels nominal reserve would result in 670 million barrels of uncertainty. However, 1-pu uncertainty in a 5-pu nominal formation with a reservoir of the same nominal size would amount to 2 billion barrels of uncertainty.³⁹² Some major reservoirs have extremely low porosity values and similar or larger nominal reserve volumes, making a low-pu uncertainty even more essential.

To put this in practical terms, it is noted that the United States had 36.5 billion barrels in oil reserves in December 2013.³⁹³ These reserves were located in various reservoirs around the country, each with likely a different nominal porosity. Assuming an average (but fictitious) nominal porosity of 30 pu for the total United States reserve, even a 1-pu error would result in an uncertainty of 1.22 billion barrels, which, at \$70 per barrel, would amount to \$85.4 billion. Positive errors, or overestimates, result in lost investments by completing wells that will not prove to be economically viable. Negative errors, or underestimates, lead to zones being passed over in favor of areas that appear more lucrative. Therefore, accurate porosity estimates are essential to determining which areas are economically viable for further development for production.

Rock permeability determines the ability of the fluid to flow for production. The permeability is determined using core samples. Lithology, or rock type, affects density, porosity, and permeability. Delineating sand zones from shales is important to identify potentially productive zones. In addition, rock mechanical properties, formation fluid type, and mineralogy are important parameters in an unconventional or complex reservoir. Rock mechanical properties are important in drilling practices, especially in complex rock types. In unconventional reservoirs (such as shale oil/gas reservoirs), mineralogical properties to differentiate between various sources of carbon that may be present become important. There is no direct logging method yet to quantitatively measure the permeability versus depth, though some log measurements can provide a permeability indicator. Rock mechanical properties, fluid types, and mineralogy are determined using log data, generally benchmarked against core data.

³⁹¹ 1 pu = 1%.

³⁹² Badruzzaman, et al., “Radioactive Sources in Petroleum Industry: Applications, Concerns and Alternatives,” SPE 123593, Presented at SPE Asia Pacific Health, Safety, Security, and Environment Conference and Exhibition, August 4-5, 2009, ISBN: 978-1-55563-260-1.

³⁹³ U.S. Energy Information Administration (EIA), Form EIA-23L, Annual Survey of Domestic Oil and Gas Reserves, 2013.

Commercially Available Well Logging Technology — Isotopic Techniques

Radioisotopes have been used successfully in well logging for decades to determine the geological parameters around a well. The two most common isotopes are americium-241 (Am-241) and cesium-137 (Cs-137), and their applications in well logging are described below.

Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization summarizes various isotopic techniques, the measured parameters, and associated petrophysical interpretation. The Table, adopted from a recent DOE/NNSA-supported study,³⁹⁴ also addresses the attributes associated with the interpretation and depth of investigation of the various techniques.

³⁹⁴ Badruzzaman, et al., Scoping Study on Developing Alternatives to Radionuclide-based Logging Technologies, LLNL-TR-679101, October 30, 2015.

Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization

Measurement Technique	Measured Parameters	Key Interpretation	Comment	Depth of investigation
Cs-137: 662 keV gamma rays	Intensity versus energy	Density-based porosity Gas identification in combination with neutron porosity Photoelectric for lithology Rock image	Typically, two scintillation detectors; one company has three-detector device. Density accuracy is .015 g/cc in both clean formations and shale	2-4 inches
Am-241/Be neutrons	Total neutron counts and ratio of counts in two detectors	Apparent porosity: Gas; shale (clay) versus sand differentiation, especially when natural gamma ray is unusable; lithology Lithology is input to porosity and saturation.	Typically, a dual-detector device Also helps make casing-cement placement decisions	~ 18 inches
Am-241/Be spectra	Neutron capture spectra	Mineralogy	Typically, a single detector. Cannot identify carbon (C), potassium (K) at all or magnesium (Mg) well Logging speed 200 ft/hr ³⁹⁵	~ 18 inches
Electrical -Induced - Natural	Resistivity, induction Spontaneous potential	Saturation Permeability indication (sometimes)	Rocks and oil have low conductivity Saline water has high conductivity	Tens of feet
Natural gamma ray	Total gamma ray counts Spectra (K, thorium (Th), uranium (U))	Shale (clay) versus sand; clay volume Delineate shale radioactivity from 'hot' sands	K and Th gamma rays are shale indicators U gamma rays indicate fluid movement U gamma rays often are a useful indicator of shale resource	Varies: 8 -18 inches
Acoustic	Transit time, intensity, attenuation, and dispersion	Porosity, lithology indicator, seismic tie, Rock anisotropy Rock mechanical properties, Permeability estimate Fluid/hydrocarbon identification, viscosity	Centered in hole Correlation-based Inapplicable in unconsolidated sands	Can be a few feet
Nuclear Magnetic Resonance (NMR)	Polarization and relaxation times, etc.	Liquid porosity: lithology- independent; Permeability estimate Viscosity Fluid typing	Signal/noise ratio (SNR) issues Current wireline tool logging speed: 200 ft/hr Typical accuracy ~2 pu Challenged in: heavy oil, nano pores in unconventional reservoirs; presence of paramagnetic substances	Not straightforward. (inch to feet), but highly dependent on type of reservoir, geologic impurities, and operator specifications

³⁹⁵ Compared to 1800 ft/hr for other wireline techniques.

Gamma Ray Density and Porosity, and Lithology Measurements - Cesium-137

The density of a geological formation around the well is typically determined using a device with a cesium-137 source emitting 662 keV gamma rays and usually two scintillators that detect the backscattered radiation. Shielding material is placed between the source and the detectors to prevent gamma rays from the source directly reaching the detectors. These sources are typically 1-3 Ci in a non-soluble form. The cesium-137 sources are often small, with the typical radiological source material about the size of a pencil eraser. The containment unit is typically much larger, with a cylinder about 4 inches long and 1 inch in diameter.³⁹⁶

During logging, the gamma rays from the source undergo Compton scattering³⁹⁷ in the surrounding rock and may undergo photo-electric absorption as their energy-level reduces. The scintillators record the gamma ray intensity versus energy. The intensity in the high-energy range reflecting the Compton scattering is a direct measure of the formation density. The computed density is used to determine the porosity.

The cesium-137-based density is accurate to within ± 0.01 gm/cc in both clean formations and shales. This translates into a porosity accuracy of better than ± 1 pu which is the most accurate log-based measure of porosity. However, it is a shallow measurement (only 2-4 inches radially).

Neutron Sources — Americium-beryllium (Am-241/Be) — For Porosity and Lithology Measurements

Neutron sources for well logging are typically a mixture of americium-241 and beryllium (Am-241/Be). These neutron sources with two helium-3 (He-3) detectors are among the most common and reliable technologies used in well logging. These devices are used to determine the neutron porosity of geologic formations. The alpha particles emitted from americium-241 collide with the Be-9 nuclei in a fusion reaction,³⁹⁸ which produces a broad spectrum of neutrons.³⁹⁹ Other alpha emitters, such as plutonium-238 (Pu-238) and radium-226 (Ra-226),⁴⁰⁰ have also been utilized in neutron porosity tools.

The neutrons emitted from Am-241/Be or other radioisotope-based neutron sources undergo primarily elastic scattering with hydrogen nuclei in the formation to moderate (i.e., reduce the kinetic energy, or slow down) to thermal energies. The thermalized neutrons then diffuse and are finally absorbed by the surrounding geologic media. The ratio of count rates in the two detectors is used to estimate the porosity and is calibrated to compute what is termed the “apparent” neutron porosity. This is a measure of the hydrogen index of the formation. This qualifier arises from the fact that hydrogen nuclei are present in water or hydrocarbons in the pore space and also in clay-bound water in the rock. Thus, only in clean, water-filled formations can the neutron porosity be viewed as a measure of the actual rather than apparent formation porosity, matching the density-based porosity. Due to the relative presence of hydrogen, the apparent neutron porosity in shales would be higher than in water-filled sands, but lower than in gas sands.

The above attributes lead to key interpretations of apparent neutron porosity noted in Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization: locating gas, determining

³⁹⁶ Badruzzaman, et al., *Radioactive Sources in Petroleum Industry: Applications, Concerns and Alternatives*, SPE 123593, Presented at SPE Asia Pacific Health, Safety, Security, and Environment Conference and Exhibition, August 4-5, 2009.

³⁹⁷ The scattering of a high-energy photon by a charged particle, usually an electron.

³⁹⁸ ${}^9\text{Be}(\alpha, n){}^{12}\text{C}$.

³⁹⁹ There also exists the potential to produce neutrons from the less common $\text{Be}(\alpha, \alpha' n)$ reaction and $\text{Be}(n, 2n)$ reactions.

⁴⁰⁰ These isotopes are mixed with beryllium, taking the forms Pu-238/Be and Ra-226/Be respectively.

lithology, and differentiating between shales and sands, especially when natural gamma ray logs cannot be used. Together with the cesium-137-based density values, the neutron porosity measure provides the basis for determine the presence of natural gas.

The type of petrochemical exploration determines the activity of the Am-241/Be source. Hydrocarbon exploration requires larger sources ~15+ Ci for compensated neutron porosity. Natural gas exploration can be accomplished with smaller 5 Ci sources used in correlation tools. A typical small well-logging company is likely to have a range of Am-241/Be sources positioned geographically to support its customers.

Neutron Sources — Americium-beryllium (Am-241/Be) — For Mineralogy Measurements

Beginning in the mid-1990s, tools with an Am-241/Be source and usually a bismuth germanium oxide (BGO) detector were introduced to perform neutron capture spectroscopy⁴⁰¹ measurements to determine the mineralogical components of the rock. Typically, thermal neutrons are absorbed (i.e., captured) by the surrounding earth and characteristic gamma ray are emitted. Elemental yields are determined from the spectral data utilizing so-called closure relations. The neutrons produced by Am-241/Be sources are typically of insufficient energy to be used in chemical analysis of inelastic neutron collision spectrometry.

One major objective of neutron capture spectroscopy has been determination of the clay content of rocks. Research assessing a large number of rock samples using infrared mineralogy and chemical composition analysis had shown a strong linear relationship between aluminum (Al) and total clay concentration. It is difficult to measure directly using the spectral data of the aluminum which provides the clay signature. However, studies by Herron and Herron⁴⁰² found that correlations consisting of capture-derived elemental yields of silicon, calcium, and iron can be used to estimate (or emulate) the aluminum concentration, thereby avoiding the need for direct measurement of aluminum. Two such tools have been marketed.⁴⁰³ In addition, neutron-capture spectra cannot show the presence of carbon (C), a major element of interest in petroleum applications, or magnesium (Mg), which would allow a delineation to major reservoir rocks, limestone, and dolomite. Al, C, Mg, etc., are particularly important in exploring unconventional resources (e.g., shale gas and shale oil).

Isotopic Neutron Sources Other Than Americium-241

As mentioned above, isotopic neutron sources other than Am-241/Be may be used for porosity and lithology measurements. These isotopes would have a similar risk profile to Am-241/Be. One example would be the use of other actinide beryllium neutron sources, such as Pu-238/Be, which also take advantage of fusion and other nuclear reactions to produce neutrons. The neutron energy spectrum of other actinide-beryllium sources is similar to that of Am-241/Be, but with some subtle differences. These other sources would have similar or more restrictive security controls to Am-241/Be sources.

Another type of isotopic neutron source sometimes considered for well logging purposes is isotopes that produce neutrons by spontaneous fission decay. Unlike most chemical neutron sources (i.e., Am-241/Be or Pu-238/Be), which produce neutrons from a low-probability nuclear reaction following radioactive decay,

⁴⁰¹ The (n,γ) reaction is when a neutron is absorbed by a target nucleus and emits a gamma ray. Many isotopes have signature gamma ray emission from a thermal (n,γ) reaction.

⁴⁰² Herron, S.L. and M.H. Herron, *Quantitative Lithology: An application for Open- and Cased-hole Spectroscopy*, Trans, SPWLA 37th Annual Logging Symposium, Paper E, 1996.

⁴⁰³ Herron, S. L. and M. H. Herron, *Quantitative Lithology: An application for Open- and Cased-hole Spectroscopy*, Trans, SPWLA 37th Annual Logging Symposium, Paper E, 1996; Galford et al., A new neutron-induced gamma ray spectroscopy tool for geochemical logging, SPWLA 50th Annual Logging Symposium, Paper X, 2009.

spontaneous-fission neutron sources, such as californium-252 (Cf-252), produce the neutrons directly from a fission reaction. The neutrons are emitted isotopically and continuously, like all other isotopic neutron sources. However, spontaneous-fission sources will have a different neutron spectrum than traditional chemical neutron sources, which rely on alpha-emitting isotopes for neutron production: Their spectra would be somewhat similar to the neutron spectrum found in some nuclear reactors. Much like the electrical deuterium (D)-tritium (T) (D-T) neutron sources described below, further R&D efforts would be required to relate this emitted spectrum and the subsequent reflected nuclear emissions to known lithographies.

Spontaneous-fission isotopic sources are typically relatively short-lived, with half-lives of less than a few years. These isotopes are also typically the heavier transuranic radioisotopes and are not produced on large scales. The current global production rate may not be adequate for large-scale industrial applications such as well logging.

Californium-252 is a spontaneous fission source which produces the neutrons directly from the fission reaction. The neutron yield from californium-252 is much higher than Am-241/Be sources. Equivalent commercial sources may contain 27 mCi of californium-252 versus 16 Ci of Am-241. A californium-252 device was developed by a medium-sized company,⁴⁰⁴ but the company was acquired by a large logging company and no further development of the tool is apparent.

Commercially Available Well Logging Technology — Non-Isotopic Techniques

Radionuclide-based logging tools pose security and source risks. As previously mentioned, a Scoping Study was conducted with DOE NNSA support to note or assess: 1) source risks; 2) current state of down-hole logging technologies; 3) key requirements alternative technologies must meet to be of replacement quality; 4) performance of tested alternatives and research gaps; 5) untested but promising alternatives; and 6) non-technical roadblocks to implement alternatives.⁴⁰⁵ In this section, only technological aspects of alternatives are discussed.

A list of non-isotopic well logging techniques can also be found in Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization. These techniques include electrical measurements, natural gamma ray detection, acoustic, and NMR. Each of these techniques will be described in more detail later in this section.

Electrical Resistance for Saturation

Another type of isotopic neutron source sometimes considered for well logging purposes is isotopes that produce neutrons by spontaneous fission decay. Unlike most chemical neutron sources (i.e., Am-241/Be or Pu-238/Be), which produce neutrons from a low-probability nuclear reaction following radioactive decay, spontaneous-fission neutron sources, such as californium-252 (Cf-252), produce the neutrons directly from a fission reaction. The neutrons are emitted isotopically and continuously, like all other isotopic neutron sources. However, spontaneous-fission sources will have a different neutron spectrum than traditional chemical neutron sources, which rely on alpha-emitting isotopes for neutron production: Their spectra would be somewhat similar to the neutron spectrum found in some nuclear reactors. Much like the electrical

⁴⁰⁴ Valant-Spaight et al, "Field Examples with a Slim LWD Density/Neutron Instrument Containing a Californium-252 Neutron Source and Three Neutron Detectors," Proc. 47th SPWLA Annual Logging Symposium, Paper CCC.

⁴⁰⁵ Badruzzaman, et al., Scoping Study on Developing Alternatives to Radionuclide-based Logging Technologies, LLNL-TR-679101, October 30, 2015.

deuterium (D)-tritium (T) (D-T) neutron sources described below, further R&D efforts would be required to relate this emitted spectrum and the subsequent reflected nuclear emissions to known lithographies.

Spontaneous-fission isotopic sources are typically relatively short-lived, with half-lives of less than a few years. These isotopes are also typically the heavier transuranic radioisotopes and are not produced on large scales. The current global production rate may not be adequate for large-scale industrial applications such as well logging.

Natural Gamma Ray: Total and Spectral

The gamma rays from naturally occurring isotopes present in the formation—potassium-40, thorium-232, and uranium-238 (K-40, Th-232, and U-238, respectively)—can be recorded in scintillators either as total counts or as spectra. Typically, background natural gamma ray counts are considerably higher in shales, which are non-productive for petrochemicals, than in clean reservoir rocks (e.g., sandstone, limestone, and dolomite). The difference is used to distinguish between the two types of rocks. The information is used to decide well placement and completion. Correlations constructed using the natural gamma ray signature in shales versus clean formations are used to compute the shale volume fraction to account for non-reservoir rocks in porosity estimate.

Well loggers will often use low-activity radioisotope calibration sources containing K-40, Th-232, and U-238 (called KTh calibrators) in the field to calibrate the scintillation counters. These sources are often low activity and were not identified as a risk driver in the National Academies study.

Acoustic Techniques

Seismic methods are best used to determine generally what reserves may lie underground across large geological extents. Seismic surveys are more common in exploring newly discovered formations. If seismic surveys prove positive, wells are drilled and downhole data are acquired through logging measurements performed either in the wireline mode or in LWD mode. Often, rock samples are acquired at discrete formation locations to perform core analysis in a laboratory. Core data are used as benchmarks.

Seismic surveys can be broken into two subcategories: passive seismology and reflective seismology. Passive seismology relies on natural movements in a geologic formation. Measurements are made by distributing multiple portable seismometers across a range of hundreds of meters for a period of up to several days. The seismometers detect the natural movements of the ground and use time stamps and frequency analysis of the vibrations (i.e., sound waves) to construct an estimate of the underground geology, including the potential for presence of fluids.

Reflective seismology uses a controlled active artificial source of sound waves to interrogate the ground—a process akin to echolocation in animals or sonar used by maritime vessels. The source of the artificial waves is often a controlled concentrated explosion or an air gun. The reflected seismic waves are then used to determine the local geology in a similar way to passive seismic methods. Reflective seismic methods are more accurate than passive seismic methods; however, they are also louder, more damaging to the environment, and more expensive than passive seismic measurements, which have minimal environmental effects.

Acoustic sources allow petrophysical measurements similar to the seismic methods used to bulk characterize local geology found above. A probe consists of an acoustic source and a receiver or an array of receivers. The probe lowered into a borehole emits low-frequency sound waves, and reflections off the surrounding medium are recorded in the receivers. In Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization it is noted that the technique allows determination of the porosity, lithology, and supply estimates of the permeability, fluid identification, and viscosity. For example, porosity is

related to transit time; however, the resulting relations depend on the rocks' mechanical properties, and may not be linear. As noted in Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization, acoustic porosity techniques do not work in unconsolidated sands. Some of the world's major reservoirs are in unconsolidated sands.

The accuracy of acoustic porosity is on the order of 2-4 pu. The depth of investigation is several feet from the probe, making it one of the farthest-reaching interrogative options for well logging.

Under complex geological conditions, acoustical measurements may be able to fill in the gaps left by traditional nuclear measurements. As noted in Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization, the acoustic data can supply information about the surrounding rocks' mechanical properties, which is useful when drilling in non-traditional environments and in places where hydraulic fracturing is needed for oil extraction.

Nuclear Magnetic Resonance Logging

This technique as used in well logging is based on the response of hydrogen nuclei in a fluid to magnetic and radiofrequency excitations. Typically, the magnetic field polarizes the hydrogen nuclei (protons). This basic technology was first developed in the 1950s and is most prolifically used in the medical industry, where it is called magnetic resonance imaging (MRI).

Contrary to its name, NMR technology does not actually use nuclear or radiological technology. Instead, it employs two electro-magnets, with the first magnet projecting a powerful magnetic field and the second magnet creating a weaker oscillation in that field. This perturbs and polarizes the hydrogen nuclei within range. The nuclei are modulated with a transverse radio frequency field, which reflects a signal back to the receiver in the probe. The time-scale length for polarization (or relaxation by withdrawing the field) is related to porosity.

In Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization, it is noted that in well logging, NMR techniques allow determination of porosity, fluid types—an indication of permeability—and a measure of fluid viscosity. There does not need to be any assumption of the rock lithology to determine porosity. However, the temporal cut-off points used to measure polarization of the hydrogen nuclei in different rock types do depend on the rock type (i.e., lithology). Fluid typing by NMR techniques is particularly valuable; traditional nuclear techniques are less able to achieve this.

The disadvantage of using NMR technology is that in wireline logging there is a slow interrogation technique, with a typical speed of current generation of NMR tools being 200 feet per hour; standard logging speeds are approximately 1,800 feet per hour.⁴⁰⁶ Time is a valuable commodity in oil exploration, and the use of slower technology is a major impediment to widespread use. The logging speed can be increased, but this may come at the expense of complete polarization of surrounding nuclei in the rock matrix, resulting in a lower resolution and signal-to-noise ratio. It may be possible to achieve the same resolution at higher speeds, but it would require a physically larger probe that may exceed current volumetric restrictions in place in wells. Recent developments indicate that technology advances may mitigate some of these limitations. NMR cannot supply lithology, and the lithology from acoustic is not as accurate as that from radionuclide tools. Neither can determine mineralogy.

The NMR technique faces a number of inherent physical limitations such as in heavy oils which have high viscosity, in nano-pores, and in the presence of paramagnetic substances. The current porosity error for

⁴⁰⁶ Akkurt, Ridvan, et al., "Towards Everyday-NMR: An Operator's Perspective," *Petrophysics*, 2009, 50 (6): 495-510, SPWLA-2010-v51n3a1.

NMR is 2 pu, which is greater than the current nuclear technology. It may be possible to improve on this error with improvements in signal/noise ratio.

NMR technology requires skilled operators and a good interpretation system to produce optimal results. Besides capability and accuracy, the major issues of replacing nuclear logging tools are cost and complexity of acoustic and generator-based tools. Today, NMR technology is typically only used by larger firms, with limited adoption by smaller firms. Cost is an influence of technology choice.

Commercially Available Well Logging Technology — Potential Alternative Technologies

There are several existing technologies that might serve as alternative techniques to isotopic sources for well logging. Recall from Table 7.1: Conventional Commercial Well Logging Techniques for Reservoir Characterization that acoustic and NMR techniques can determine a porosity, in addition to the unique parameters they supply. Thus, these two techniques have been suggested by some as alternatives to radionuclide-based porosity techniques. However, as discussed, both techniques have significant limitations to overcome before they are validated as replacements. Acoustic techniques are generally available from several service providers, while NMR techniques are available mainly through major logging companies.

Even when NMR and acoustic techniques are used, other technologies will still be required to identify the lithology and mineralogy of a well. Currently, this is determined with isotopic neutron sources, but accelerator-based technology may also be used to generate neutrons. Table 7.2: Logging Techniques Marketed as Alternatives to Radionuclide-based Tools lists the currently marketed alternative techniques and their states for various key attributes.

Table 7.2: Logging Techniques Marketed as Alternatives to Radionuclide-based Tools⁴⁰⁷

	Acoustic	Nuclear Magnetic Resonance (NMR)	Deuterium-tritium (D-T) Neutron Tool	Inelastic n- gamma Density (INGD) via (D-T) Neutron Generator
Density accuracy*	N/A	N/A	N/A	±0.025 gm/cc in clean formations and ±0.045 gm/cc in shales
Porosity accuracy**	2-4 pu+	2 pu+: can improve	1 pu in many cases, but with special design and processing	2 pu in clean formations and 4.5 pu in shale+
Lithology	Limited	No	Yes	Not clear
Mineralogy	No	No	Yes, with both inelastic and capture data with scintillator included in hardware++	Unlikely
Gas	Yes	Yes	Yes	Yes
Other: Thin-bed resolution	Difficult	No	No	No
Other: Kerogen in shale resolution	No	Yes, with density	Yes, if scintillators are also included	No
Mitigate legacy data issue?	No	No	Yes, with special processing	Limited, unlikely
Service providers	Multiple	Limited to major logging companies	One service company	One service company
Cost	Moderate	High	High-moderate	Not clear

Acoustic, NMR, and D-T neutron porosity have been developed for both wireline and LWD logging. For open-hole logging, INGd is only for LWD

* Cs-137-based density is accurate to within ±0.01 gm/cc

** Porosity from Cs-137 density is accurate to within ±1 porosity unit (pu). The neutron porosity from Am-241/Be neutron tools in clean water-filled formations is within 1.5 pu.

+ Reflects the cited density errors for INGd

++ Two such tools have been deployed⁴⁰⁸

⁴⁰⁷ Adapted from LLNL-TR-679101, Badruzzaman, Dowla, Chien, Antolak, Schmidt, Bakhtiari, 2015, released in 2018.

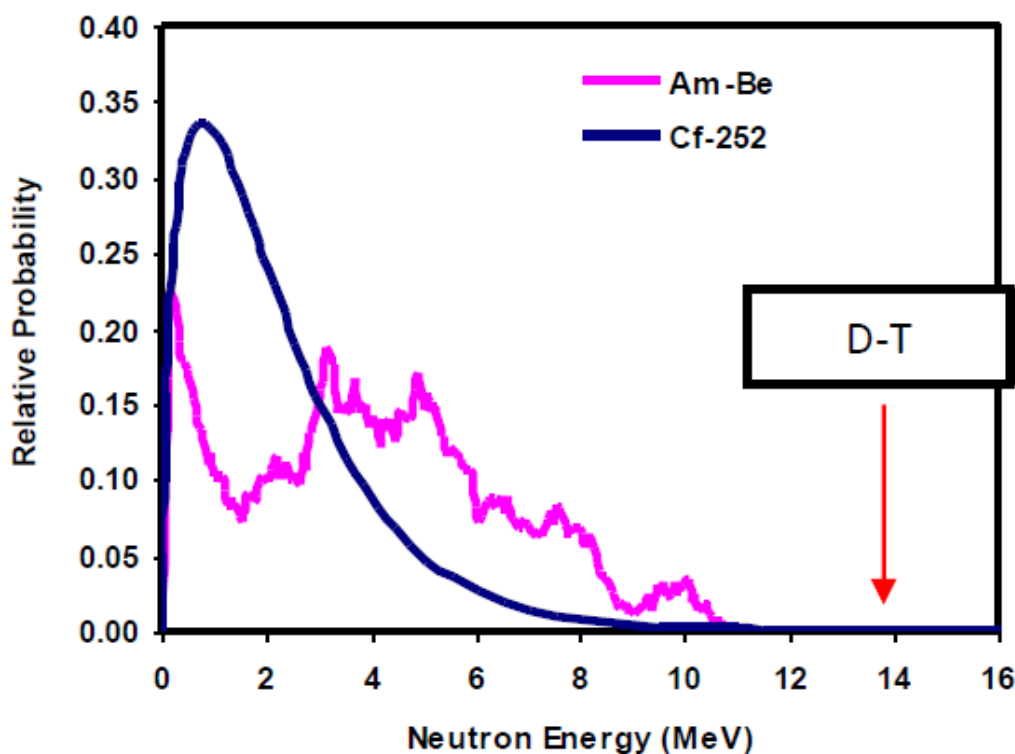
⁴⁰⁸ Pemper, R., et al, 2006, *A New Pulsed Neutron Sonde for Derivation of Formation Lithology and Mineralogy*, SPE 102770, Proc. SPE Annual Technical Conference and Exhibition, September 24-27, 2006; RJ Radtke et al., *A Capture and Inelastic Spectroscopy Tool Takes Geochemical Logging to Next Level*, Proc. 53rd SPWLA Annual Symposium, Cartagena, Columbia, June 16-20, 2012.

Deuterium-Tritium Neutron (D-T Neutron) Generators

Although traditional neutrons sources produce neutrons with radionuclides either through the (α ,n), or spontaneous fission (SF) reactions, neutrons may also be produced using particle accelerators. The most common electronic neutron source is a D-T neutron generator. In D-T generators, a projectile deuterium (d) particle is accelerated to high speeds against a target foil impregnated with tritium (t) resulting in the reaction $d(t,n)He$ to generate 14.1 MeV neutrons.

Two D-T neutron generator tools have been marketed by a major logging company, one for wireline logging⁴⁰⁹ and the other for LWD.⁴¹⁰ Libai Xu et al had examined the response of californium-252 source and D-T generator neutrons in LWD mode, by simply swapping out the neutron source.⁴¹¹ The porosity sensitivity of californium-252 neutrons was similar (but not the same) to that of Am-241/Be neutrons, whereas the porosity sensitivity of D-T neutrons were much lower. The researchers noted that, as expected, response differences arose from the differences in the neutron spectrum between the neutron sources. The californium-252 neutron spectrum is close to the Am-241/Be spectrum while the D-T neutrons are at a much higher energy. The spectrum is depicted in Table 7.1.

Figure 7.1: Am-241/Be, Cf-252 and D-T Neutron spectra⁴¹²



⁴⁰⁹ W.D. Flanagan et al., *A New Generation Nuclear Logging System*, Paper Y, Transactions, SPWLA 32nd Annual Logging Symposium, Midland, Texas, June 16-19, 1991.

⁴¹⁰ M. Evans et al., *A sourceless alternative to conventional LWD nuclear logging*, SPE 62982, in Proc. SPE Annual Technical Conference and Exhibition, Dallas, TX, October 3-4, 2000.

⁴¹¹ Libai Xu, et al., "A Comprehensive Investigation of Source Effects on Neutron Porosity Response for Logging-While-Drilling Measurements," *Petrophysics*, 51 (2010) 3: 185-198.

⁴¹² Ibid.

Inelastic n-gamma Density (INGD)

This technique utilizes gamma rays from inelastic scattering of high-energy neutrons from a D-T generator to determine a quantitative formation density. The idea originated in the 1990s as a density indicator in old cased wells with limited modern logs. In 2000, an experimental LWD tool was developed using the concept for quantitative formation density.⁴¹³ The tool was marketed in 2012. Field tests indicated that the errors in practice can be considerably greater and thus often unacceptable. An assessment of the basics of the INGD technique indicated that the coupled neutron-gamma physics of the INGD technique would make it an inherently less accurate technique than cesium-137-based density.⁴¹⁴ The technique has been marketed by only one major logging company and for LWD applications and could only possibly be used in the absence of cesium-137 devices⁴¹⁵ and a when reduced density accuracy is acceptable in estimating reserves.

D-T Generator Based n-gamma Spectroscopy for Mineralogy

Two D-T generator-based spectroscopy tools were recently marketed as alternative to Am-241/Be-based spectroscopy tools.⁴¹⁶ Inelastic neutron collision gamma spectroscopy with D-T generators allow direct detection of key elements such as carbon, aluminum, magnesium, and determination of mineralogy and total organic carbon. (n-gamma) capture spectroscopy cannot supply these.

X-ray Density

A linac tool emitting 3.5 MeV endpoint energy Bremsstrahlung spectrum was successfully field-tested in the mid-1980s to determine the formation density.⁴¹⁷ It demonstrated the feasibility of the approach as a possible replacement of cesium-137-based density. Despite this, the tool was not commercialized. One major obstacle appeared to be economics, especially due to a severe downturn in the logging industry at the time. In addition, the power requirement was high.

However, in 2018 the same major logging company reported an experimental tool with a lower energy Bremsstrahlung x-ray source.⁴¹⁸ The source utilizes a 350 keV endpoint energy x-ray device and several advanced scintillators. The method is based entirely on photon physics, as is the cesium-137-based density, and appears promising but further assessment is needed to establish if it can replace the cesium-137-based density.

Neutron Generators Other Than D-T for Neutron Porosity

Several other neutron generators have been proposed for use in neutron porosity tools. These include D-D (deuterium projectile and target) and D-⁷Li (deuterium projectile and lithium-7 target), which are fusion generators, and a dense plasma focus (DPF) alpha particle accelerator with a beryllium target. D-D generates 2.45 MeV neutrons and D-⁷Li generates a broad spectrum of neutrons similar to the Am-241/Be

⁴¹³ Evans, M., et al., *A sourceless alternative to conventional LWD nuclear logging*, SPE 62982, in Proc. SPE Annual Technical Conference and Exhibition, Dallas, TX, October 3-4, 2000.

⁴¹⁴ Badruzzaman, Ahmed, "An Assessment of Fundamentals of Nuclear-based Alternatives to Conventional Chemical Source Bulk Density Measurement," *Petrophysics*, 55 (2014) 5, 415-434.

⁴¹⁵ The use of a strong Cs-137 source may mask the less common gamma rays emitted during the (n,γ) reaction.

⁴¹⁶ Pemper, R., et al, 2006, *A New Pulsed Neutron Sonde for Derivation of Formation Lithology and Mineralogy*, SPE 102770, Proc. SPE Annual Technical Conference and Exhibition, September 24-27, 2006; RJ Radtke et al., *A Capture and Inelastic Spectroscopy Tool Takes Geochemical Logging to Next Level*, Proc. 53rd SPWLA Annual Symposium, Cartagena, Columbia, June 16-20, 2012.

⁴¹⁷ King III, G., et al., "Density Logging Using An Electron Linear Accelerator as the X-Ray Source," *Nuclear Instruments and Methods in Physics Research* B24/25, 990-994, 1987.

⁴¹⁸ Simon, Matthieu, et al., "A Novel X-Ray Tool for True Sourceless Density Logging," *Petrophysics*, Vol. 50, No. 5, October 2018.

spectrum. The DPF accelerator generates a neutron spectrum that is almost identical to Am-241/Be neutron spectrum, as seen in Figure 7.3.

Figure 7.2: Neutron spectra from ${}^7\text{Li}(d,n){}^8\text{Be}$, D-D, D-T, and ${}^{241}\text{Am}$ -Be ⁴¹⁹

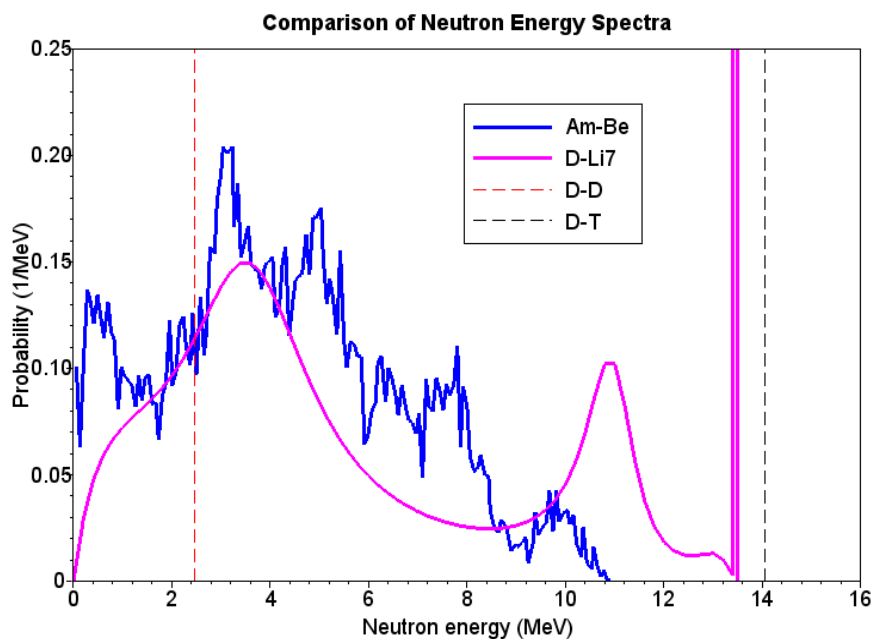
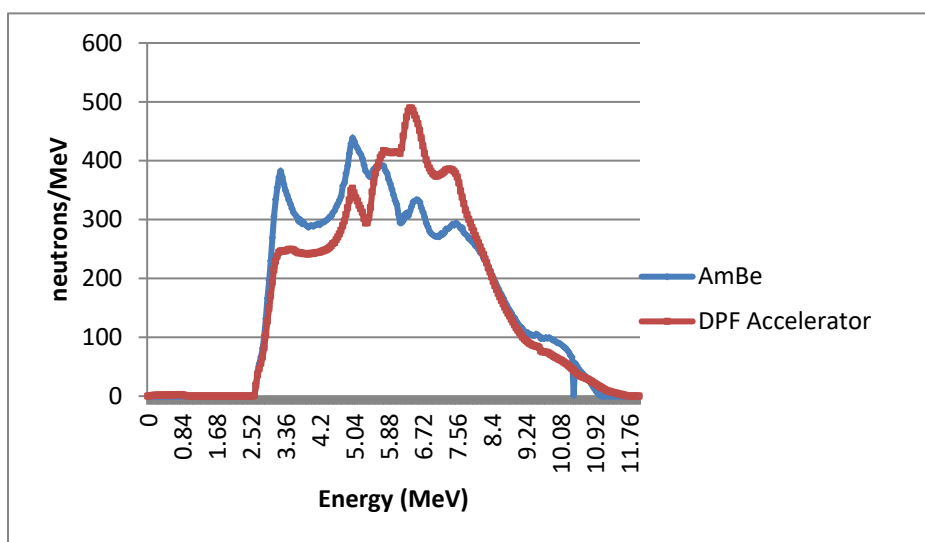


Figure 7.3: Comparison of Neutron spectra from AM-Be and DPF neutron sources ⁴²⁰



⁴¹⁹ Adopted from LLNL-TR-679101, Badruzzaman, Dowla, Chien, Antolak, Schmidt, Bakhtiari, 2015, released in 2018.

⁴²⁰ Adopted from LLNL-TR-679101, Badruzzaman, Dowla, Chien, Antolak, Schmidt, Bakhtiari, 2015. Original from Schmidt A, Tang V, and Welch D, 2012, "Fully Kinetic Simulations of Dense Plasma Focus Z-Pinch Devices," Physical Review Letters, 109 (20): p. 205,003.

A 2019 paper described a study on the basics of these generators to assess their potential performance against Am-241/Be and D-T neutrons under a number of formation and well conditions.⁴²¹ The paper noted that none of the neutron generators offered a clear advantage over the others and designers would need to make tradeoffs on what they want to utilize these tools for, namely neutron porosity, mineralogy, or both. The authors concluded that in view of their spectra, DPF could be an almost exact replacement of Am-241/Be for neutron porosity, but it is still at a research phase. D-D generators would offer greater porosity sensitivity than with Am-241/Be neutrons while D-⁷Li would offer similar porosity sensitivity. The neutron yield of both generators would need to increase nearly 100-fold to for acceptable statistics. D-D generators would supply only neutron capture-based spectroscopy for mineralogy. (D-⁷Li) may provide inelastic neutron scattering but further assessment is needed.

Multiple Parameters with a Single Neutron Generator.

The same paper noted that the mineralogy determination by DPF neutron tool would be similar to that from Am-241/Be (i.e., capture-based) and thus limited, as would be the case for D-D neutrons. Only D-T generator neutrons would provide a more complete mineralogy.⁴²² Thus, if a multiple-parameter tool (providing neutron porosity, mineralogy, saturation, and a poor-man's density, namely the INGD) with a single generator is desired, the D-T generator may be the best option, despite its limitations. One major logging company has deployed such a tool, but only for LWD.⁴²³

Technology Purchase and Replacement Considerations

The following section outlines considerations potential buyers would base their purchase/replacement decisions on, including lifecycle costs, device requirements, and disposal.

Lifecycle Technology Costs

The approach to determine the lifecycle cost for the technologies outlined above is complicated and tied to the operational duration required to conduct geologic interrogations in complex and highly variable environments. Therefore, it may be more applicable to describe the cost per well logging job, including amortizing up-front and back-end costs, than it would be to describe total lifecycle costs. The baseline cost for onshore well logging activities using Am-241/Be sources is approximately \$3,000 to \$35,000 per job depending on depth and investigation type. Some high-intensity vertical jobs may total up to \$75,000 to \$100,000. A typical vertical hydrocarbon Triple Combo, which encompasses 80 percent of all jobs performed, would run approximately \$7,000.⁴²⁴ Horizontal hydrocarbon logs are more expensive and are logged with small memory tools and run from \$35,000 to \$100,000. All the aforementioned costs include the rigging, results analysis and decision time, and labor.

Offshore logging activities are much more expensive. A Quad-Combo costs approximately \$150,000 per job.⁴²⁵ The cost can increase to \$750,000 if pump-out pressure and fluid-sampling operations are required. An important economic cost for offshore activities is worker time. Rigging and labor costs add up quickly, so

⁴²¹ A Badruzzaman, et al., "Neutron Generators as Alternatives to Am-Be Neutron Sources in Well Logging: An Assessment of Fundamentals," *Petrophysics*, Vol. 60, No.1, pages 136-170, 2019.

⁴²² Ibid.

⁴²³ M. Evans et al., *A sourceless alternative to conventional LWD nuclear logging*, SPE 62982, in Proc. SPE Annual Technical Conference and Exhibition, Dallas, TX, October 3-4, 2000; Nicole Reichel et al., *Neutron-Gamma Density (NGD): Principles, Field Test Results and Log Quality Control of a Radioisotope-free Bulk Density Measurement*, Paper GGG, Proc. SPWLA 53rd Annual Symposium, Cartagena, Colombia, June 16-20, 2012.

⁴²⁴ A string of instruments that measure electrical resistivity, porosity (via neutrons), and density.

⁴²⁵ A string of instruments that measure electrical resistivity, porosity (via neutrons), density, and acoustics.

it is best that any replacement technology log at a rate similar to that of existing radiological methods, which in some cases may also be the speed of drilling the borehole itself.

Data-analysis time and decision-making time are related factors. It is not cost efficient to have an idle workforce awaiting instructions on how to proceed while analysis is being completed; therefore, any data should be readily understandable and amenable to timely decision-making. Legacy techniques, such as those using radioisotope techniques, are the current benchmark for decision-making time.

Finally, the technology should be highly reliable. Any maintenance and repairs to the technology must be factored into the cost of doing a job. Should a piece of equipment fail during operation, it can cost valuable time to recover it from the borehole, repair it, and redeploy it for logging while other laborers are sitting idle. For this reason, passively operating technology—such as current nuclear and radiological sources—and those without moving parts are preferred.

Another important factor to consider is that in the United States logging industry, about 70 percent of the logging units are from small firms that mostly use established nuclear and radiological technology. Analysis equipment is based upon that technology. Contrary to popular belief, well logging has narrow profit margins and smaller firms lack the resources to perform R&D in house, relying entirely on legacy methods. While it is possible that R&D could be conducted by the United States government—potentially in cooperation with private industry and that products of that research could be shared openly—operator training and purchase of new supporting equipment would still need to be included in a cost estimate.

The cost of Am-241/Be sources are proprietary and will vary but they average around about \$10,000 per curie. A 2 Ci cesium-137 is around \$35,000. These costs do not reflect other related equipment or training.⁴²⁶ There are additional safety and security costs associated with possessing radiological materials, which can be estimated to be around \$20,000 per year. On the other hand, these tools are compatible with existing analysis tools used and owned by most well loggers. This is beneficial for small exploration firms who have limited equipment budgets. Furthermore, the science and data are well understood so R&D costs have been costed in the past. Again, this is essentially beneficial for small exploration firms that cannot afford to undertake expensive R&D for what may already be a limited, marginally profitable well.

The cost of a D-T generator is about \$50,000,⁴²⁷ which does not include the cost of training, calibration or supporting equipment. The cost for modern analysis (electrical resistivity, natural gamma ray, density) equipment strings configured for a different neutron spectrum can cost \$750k or more. When combined together, the cost could be around \$1 million. Some well loggers may require a second D-T generator and associated instrumentation on a job should the primary unit fail and require repair or replacement; this is especially important for offshore logging where the time to receive spare parts is long and daily operational costs are very high, often more than the cost of a spare generator. Therefore, the total replacement costs could exceed \$2 million. Additionally, D-T generators by definition, contain the regulated radioactive material tritium, and regulated material deuterium. It also produces neutron radiation. There are associated safety and regulatory costs associated with its use and possession.

⁴²⁶ Existing legacy equipment may be used with Am-241/Be sources.

⁴²⁷ Gilchrist, Allen, et al., *Nuclear Source Replacement- Promises and Pitfalls*, SPWLA-2011-KKK, Presented at the 51st Annual Symposium of the Soc. of Petrophysicists and Well Log Analysts, May 14-18, 2011.

Device Ability to Meet Site and Application Requirements

Well logging is a multi-faceted operation with multiple interrelated and competing requirements that can vary wildly based on application. Generally, the requirements can be broken down into several broad categories: operating environment, logging speed, density accuracy, porosity error, generator lifetime, interpretation requirements, and traceability to legacy data.

An industry survey was conducted to determine the hardware requirements for well logging.⁴²⁸ Table 7.3: Well Logging Hardware Requirements provides the key requirements as understood from current end users of well logging technology. This table provides the requirements not just for the source of interrogation, but also for the equipment used to collect the data. While the isotopic sources themselves may be able to easily survive these difficult logging conditions—especially compared with their electronic alternatives—it is important to ensure that the hardware and detectors associated with those sources also can do so.

⁴²⁸ Badruzzaman, Ahmed, et al., Scoping Study on Developing Alternatives to Radionuclide-based Logging Technologies, LLNL-TR-679101, October 30, 2015.

Table 7.3: Well Logging Hardware Requirements

Attribute		Requirement
Formation and Borehole	Temperature	75-500 °F, 600 °F in the future
	Pressure	200-30,000 psi, 40,000 psi in the future ⁴²⁹
	Vibration	1,000g shock, 5-500 Hz at 2g rms
Logging Speed		1,800 ft/hr
Borehole	Diameter and length	Diameter: 1.7-3.5 in Length: under 12ft
	Mud	Fresh or saltwater, up to 21 lb/gal with barite
	Salinity	Fresh water 30% NaCl
Accuracy	Density	+/- 0.015 g/cc or better
	Porosity	Density porosity: +/- 0.5-1 pu Neutron porosity: +/- 0.25 pu in low porosity
	Lithology	
Neutron Generator Operation	Working life	1,000 hrs
	Pulse Shape	Square, fast rise and shut off times
	Reliability	Ideally near zero, spare generator may be required
Data Quality	Precision	Equal or better than Am/Be for neutron porosity, open-hole wireline data acquisition at 1800 ft/hr Density +/- 0.015 g/cc; Neutron 1.5 pu or better
Use Cost		Equal or less than radionuclide source Onshore: \$1,000 - \$35,000/job with density/neutron and \$50,000/job with induction, \$150,000/job for LWD Job cost is complex as it includes rig time (logging speed, multiple parameters sampled), decision time (accuracy, multiple parameters sampled), labor costs, stuck and lost tools etc. Offshore rig costs are substantially higher than onshore
Physics/interpretation Complexity		Any replacement should have similar or reduced physics and interoperation times as existing technology. Accuracy should similarly be equal to or surpass existing technology
Legacy Data Compatibility		Moderate to high compatibility is desired. Must be able to replicate Am/Be lithology

Economic Obstacles to Widespread Adoption of Alternative Technology

Nearly 70 percent of the logging units⁴³⁰ in the United States well logging industry are small- and medium-sized firms that mostly use established nuclear and radiological technology. These small and mid-size companies have pricing and equipment utilization pressures because of the current price of oil, the prevalence of deep discounts within the industry, and a downturn in equipment utilization by as much as 50 percent. Due to these pressures, small and mid-size companies in the wireline logging industry cannot afford

⁴²⁹ This is equivalent to 60,000 psi at room temperature. Am-241/Be and Cs-137 sources are capable of surviving these temperature and pressures.

⁴³⁰ Logging trucks or skids.

to invest in new technologies in the current market. If a smaller company wanted to conduct research into alternate technologies, it would have to contract with a third party or receive the support of incentives from the government.⁴³¹ The remaining 30 percent of the logging units are from the four (United States-based) major multinational logging companies, which have the necessary R&D capabilities and can likely afford the costs associated with researching and developing alternative technologies. However, if the smaller companies and tool providers are priced out due to budgetary constraints, business costs for all users would increase, and those cost increases would ripple through the sector and economy.

The use of alternative technologies may also require a transition to new analysis and other supporting equipment that is both compatible with the new sources and economically viable. This equipment is often expensive and priced outside the range of profitability for most logging projects.

Disposal Costs and Considerations for Well Logging Sources

The proper disposal of radioactive materials used by the private sector is the responsibility of the licensees who benefit from them commercially. However, commercial disposal availability and security concerns related to high-activity sources have led to a temporary increase in government involvement, including the assumption of significant costs related to disposal. Cesium-137 well-logging sources are commercially disposable at several currently operational disposal facilities.

Disposal and Constraints

Due to its long half-life, americium-241 from used sources can be recycled by source manufacturers and re-sold to the marketplace in new products, reducing environmental and cost impacts of disposal. However, there are cases where final disposition is ultimately required.

Due to a lack of commercial radioactive waste disposal options for sealed sources of transuranic (TRU) elements, the Federal Government has provided the only disposal option for Am-241/Be. As a result, users were not paying the costs associated with device disposal, including transportation. The ability of the Federal Government to recover and dispose of these sources is constrained because most of the americium-241 is of foreign origin (this precludes disposal in facilities available for United States defense related wastes), and it may not be possible or desirable to return the material to the country the source came from.

Currently there is a ~30mCi limit on the disposal of americium-241 and other TRU sources at the currently operational “near-surface” (i.e., 0 to 10 meters below the surface) commercial LLRW disposal facilities. TRU sources exceeding this threshold must be disposed in a deep geologic repository, or alternative configuration providing for the long-term isolation of the waste from potential inadvertent intruders. There is no such repository operating commercially in the United States.

The DOE Waste Isolation Pilot Plant (WIPP) near Carlsbad, New Mexico, is currently the only deep geologic repository in operation the United States. WIPP is limited by federal legislation to the disposal waste generated as the result of United States atomic energy defense activities. In addition, WIPP is prohibited from accepting waste directly from commercial generators. However, for many decades, nearly all of the americium-241 used commercially in the United States was produced by DOE in conjunction with United States defense programs. As a result, these United States-origin sources, when recovered by NNSA/Off-Site Source Recovery Program (OSRP), were accepted for disposal at WIPP.

⁴³¹ Badruzzaman, Ahmed, et al., Scoping Study on Developing Alternatives to Radionuclide-based Logging Technologies, LLNL-TR-679101, October 30, 2015.

DOE began phasing out the production of americium-241 in the 1980s.⁴³² By 2003, DOE had ceased distribution of americium-241 and United States source manufacturers had exhausted the stock of United States-origin americium-241 available for the production of sealed sources. Russia emerged as the sole United States supplier. As a result, the number of disused and unwanted americium-241 devices using foreign-origin material has increased significantly and that trend is expected to continue. Without commercial or federal options for disposal of, these sources they must remain with commercial licensees in long-term storage.⁴³³

Disposal options under consideration in DOE's Final GTCC EIS⁴³⁴ may eventually address these sources. As commercial disposal options become increasingly available for these and other high-activity sealed sources, these costs will be shifted back to device licensees, adding tens or hundreds of thousands of dollars to the lifecycle costs users must consider.

⁴³² DOE has recently begun producing new Am-241 for commercial users, but this production and material utilization has not reached a stage where it would represent a significant amount of the total material requiring long term disposition.

⁴³³ Due to the aforementioned constraints, OSRP is not currently recovering disused foreign-origin Am-241, Pu-238, and Pu-239 sources.

⁴³⁴ Department of Energy (DOE), "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; DOE 2016), available at <https://www.energy.gov/em/waste-management/waste-and-materials-disposition-information/greater-class-c-low-level>.

Chapter 8: Alternative Technologies for Industrial Radiography

Introduction

Non-destructive testing (NDT) and analysis is a vital tool for industry. It is often necessary to inspect the safety and quality of both solid metal and welded systems to ensure that everything was built to design and operational specifications. This can include inspection of pipes, boilers, turbines, and structural supports. A failure of these systems can be severe, with consequences to worker and population safety, the environment, the economy, and the financial health of a project or company.

Overview

There are several types of NDT available, including, but not limited to, gamma radiography, x-ray radiography, ultrasonic, eddy current, magnetic particle, and dye penetrant. Gamma radiography is an NDT technique that produce gamma rays from a radioisotope source to perform radiography. X-ray radiography does not use a radioisotope source but instead utilizes electrically generated ionizing radiation (x-rays and bremsstrahlung radiation) to perform radiography. Both techniques can be used to find defects beneath the surface of the material.

There are other NDT applications that do not use ionizing radiation, instead employing electricity, magnetism, visible light, microwaves, millimeter waves, ultrasound waves, or chemicals to probe materials under test. Each of these techniques has advantages and disadvantages for various NDT applications. For example, some are best used to find imperfections on the surface and would not generally be considered replacement technology for gamma radiography, which can probe deep beneath the surface. This chapter will focus on NDT methods with the potential to replace or compliment gamma radiography. A reader looking for a more detailed description of the strengths of various NDT methods for finding imperfection is encouraged to read Section V of the American Society of Mechanical Engineers (ASME) Boiler and Pressure Vessel Code.⁴³⁵

Commercially Available Industrial Radiography Technology — Isotopic and Alternatives

NDT and analysis can be used to determine whether there are flaws and anomalies deep inside welds and structural materials. These technologies include gamma radiography, x-ray radiography, and ultrasonic testing.

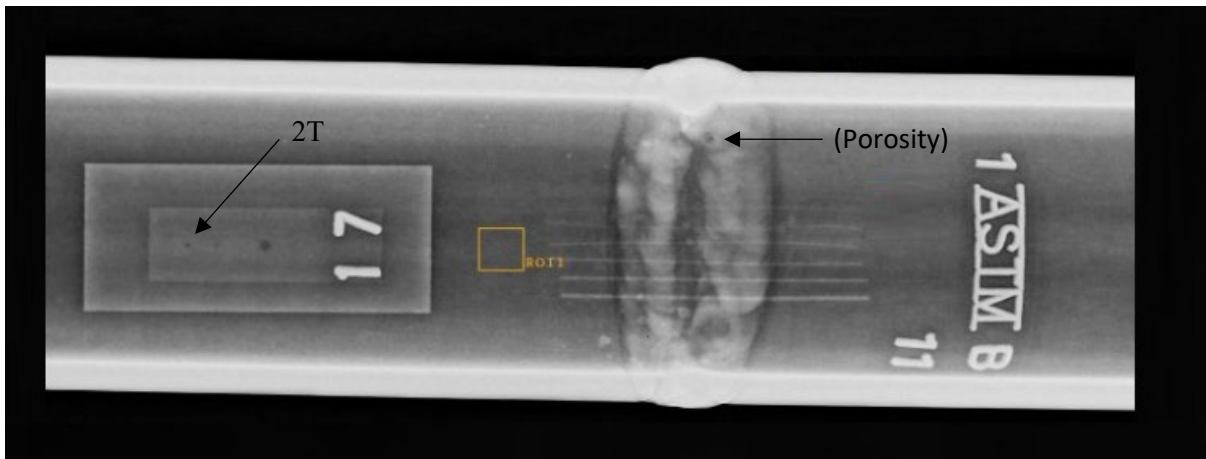
Gamma Radiography

Radiography graphically describes the mass and density (more specifically, the electron density) of a material and is a common method for examining welds and structural cement in many industrial settings. In

⁴³⁵ American Society of Mechanical Engineers (ASME), Committee on Nondestructive Examination, *ASME Boiler and Pressure Vessel Code: Nondestructive Examination*, ASME, 2017.

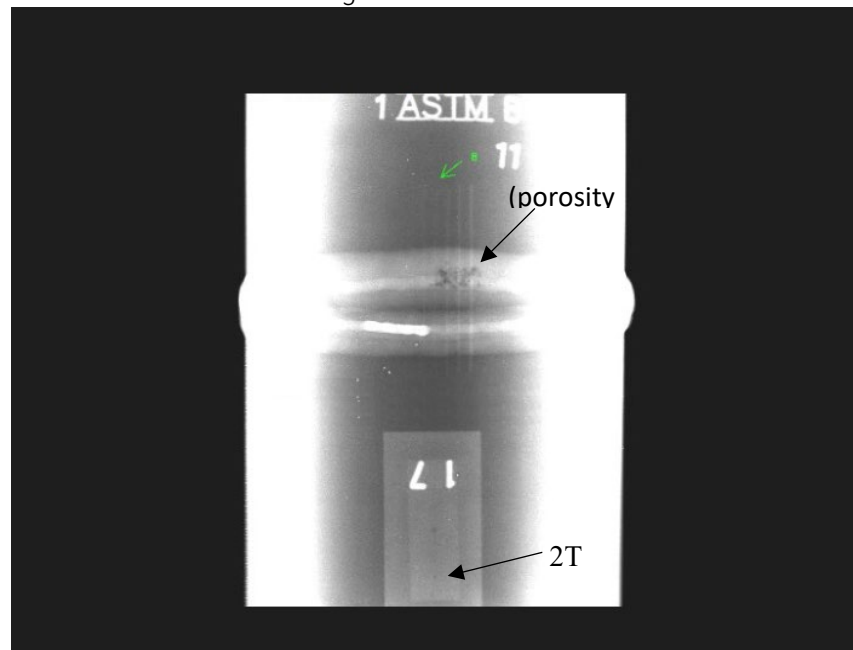
gamma radiography, a gamma-emitting radioisotope source is brought near an object to be examined. On the other side of the object is a gamma ray detector (e.g., film or storage phosphor plate or direct conversion digital detector plate). Some of the gamma rays will pass through the object but some will be attenuated—depending on the material thickness and density—resulting in variations of gamma intensity detected or interacting with the detector in the two-dimensional space behind the object. Areas with less material (or more specifically, electron clouds) will absorb or attenuate less, which will result in more gamma rays detected in the two-dimensional space behind the object. A technician or engineer can interpret these results to determine where material defects such as voids, porosity, cracks, and corrosion exist.

Figure 8.1



A 2-inch schedule 80 pipe imaged with Ir-192, overlaid with ASTM radiography standards, to indicate the quality of the radiographic technique. As an example, the “2T” hole –type indicator is pointed out to show that the imaging technique used is capable of showing a material loss of 2 percent in the area under investigation.

Figure 8.2



4-inch schedule 80 pipe images with Se-75, overlaid with ASTM radiography standards, to indicate the quality of the radiographic technique. As an example, the “2T” hole –type indicator is pointed out to show that the imaging technique used is capable of showing a material loss of 2 percent in the area under investigation.

There are several isotopes used for gamma radiography, the most common of which are iridium-192, selenium-75 (Se-75), and cobalt-60, and to a lesser extent ytterbium-169 (Yt-169). Unless otherwise mentioned, the information found in this section applies to all four isotopes.

Today, gamma radiography is oftentimes used in extreme operating conditions, remote locations, and tight spaces where technologies requiring large amounts of steady power or volume are not practical. These include, but are not limited to, remote oil pipelines that may also be in areas of extreme cold, on open-water drilling platforms or lay barges, or in tightly packed areas otherwise inaccessible to larger bulky equipment (such as refineries or other complex processing plants). For smaller, mobile components or parts, radiography may be conducted in a vault. The power generation and petrochemical sector comprise approximately 47 percent of all gamma radiography use, with the remainder spread across automotive, infrastructure (construction and inspection), manufacturing, aerospace, and other applications.⁴³⁶

Gamma radiography requires little surface preparation prior to inspection of the material⁴³⁷, nor does it require a calibration standard for use. It has been frequently used to image remote and inaccessible locations, but it still requires access to both sides of the surface or pipe being examined.

The devices are relatively quick and simple to operate and to interpret the data (typically several seconds or a few minutes), but it may take time to develop the images or to extract them from storage phosphor plates to view the results. Direct digital display detectors can provide near-real-time images. Some gamma radiography still uses film exposure to capture an image of the target structure/material; the image is then developed and assessed in a mobile dark room or a non-field location by trained personnel. There is thus typically a delay between field testing and assessment, often approximately 24 hours.

Since radiography measures how many photons pass through the material at a given location, it has natural advantages and disadvantages to the type of defect it can find. Gamma radiography cannot measure residual wall thickness or easily detect narrow planar defects that are perpendicular to the gamma ray direction (i.e., linear delamination). However, it is very effective at revealing differences in density (pores) and defects such as cracks that have a directional component in line with the gamma ray direction and shallow surface defects. It can be used to examine both solid materials and matrix materials such as concrete.

Gamma radiography—like other industrial and medical-source applications—has a regulatory burden. Licensees must comply with the NRC byproduct material use and safety regulations for gamma radiography in 10 C.F.R. Part 34. In addition, some gamma radiography devices exceed the Category 2 source security threshold. These licensees also must implement the NRC security requirements under 10 C.F.R. Part 37.⁴³⁸ There are approximately 20,000 certified radiographers in the country and approximately 500 licenses for industrial radiography. There are more than 20,000 gamma radiography sources sold worldwide every year, a quarter of which are for use in the United States.

Outside of a fixed location vault with established radiation areas, jobsite gamma radiography requires the radiography team to control access to radiographic areas during use to prevent both unnecessary worker and public exposure to radiation. While these zones have the potential to interrupt work functions, both the radiography team and the site understand these constraints and work to schedule activities accordingly.

⁴³⁶ Shilton, Mark, representing International Source Supplies and Producers Association (ISSPA), “Gamma Radiography,” presentation to the Alternative Technology Working Group, May 2017.

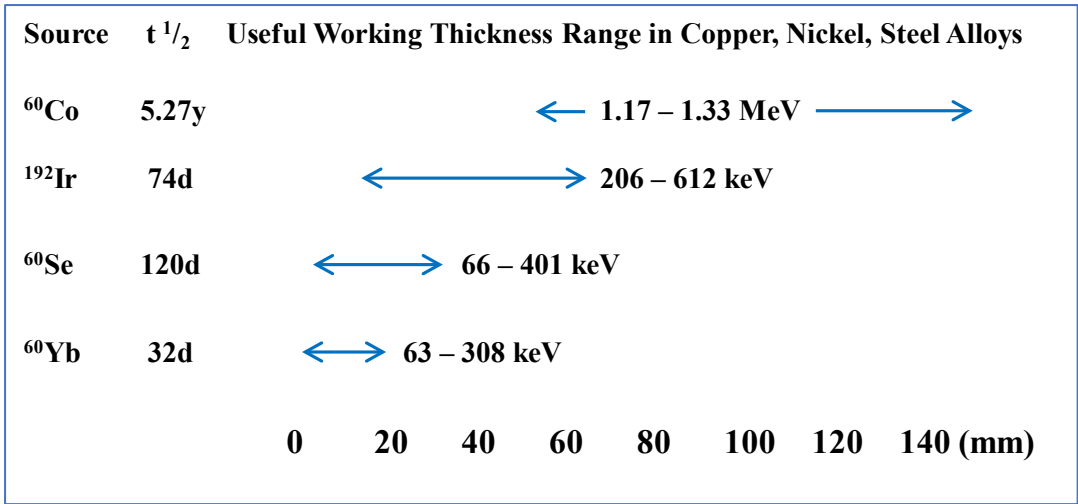
⁴³⁷ Ibid.

⁴³⁸ NRC, Industrial Radiography Licensee Toolkit, <https://www.nrc.gov/materials/miau/industrial-uses/rad-toolkit.html>.

There are additional safety and security considerations during use, as well as during storage and transport, which are described later in this chapter.

The thickness of the target material may affect which kind of radioisotope is used to perform the radiography. This is because each isotope emits different gamma ray energies that correspond to differing penetration depths. The predominant gamma ray energies used in radiography vary from 206-612 keV, with a predominant energy of approximately 370 keV. Gamma energies that are either too high or too low for a given thickness may fail to show any defects, even if they exist. Figure 8.3 shows common radiography isotopes and useful working thicknesses.

Figure 8.3: Working Thickness Range of Radiography Sources



Gamma Radiography – Iridium-192

The most common isotope used in gamma radiography in the United States is iridium-192 (Ir-192). It decays via beta emission (96 percent) to stable platinum-192 or via electron capture (4 percent) to stable osmium-192. The primary useful gamma emission is at 375 keV. Iridium is an inert noble metal which has a high melting point of 4,471 °F (2,466 °C).

New iridium-192 sources are sold in a range of activities, including some which exceed the Category 2 threshold of 21.6 Ci.⁴³⁹ As a result, these licensees must comply with the NRC security rules under 10 C.F.R. Parts 37,⁴⁴⁰ as well as the use and safety regulations for gamma radiography in 10 C.F.R. Part 34.⁴⁴¹ The iridium-192 sources must comply with “special form requirements” and 49 C.F.R. § 173.469.⁴⁴² The sources themselves are encapsulated compact cylinders of stacked thin metal disks that are typically between 0.5 millimeters and 3 millimeters in diameter. These disks are shown in Figure 8.4. The encapsulated source is placed inside a shielded handheld unit, colloquially known as a camera or projector

⁴³⁹ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008) 1.

⁴⁴⁰ Sources below the Category 2 threshold must still comply with 10 C.F.R. Parts 20 and 34, and other applicable regulations.

⁴⁴¹ U.S. Nuclear Regulatory Commission (NRC), “Industrial Radiography Licensee Toolkit,” last updated July 7, 2017, <https://www.nrc.gov/materials/miau/industrial-uses/rad-toolkit.html>.

⁴⁴² Tests for Special Form Class 7 (Radioactive) Materials, 49 C.F.R. § 173.469.

that weighs about 50 pounds and are about 13 inches by 8 inches by 9 inches. The camera functions as robust shielding, generally depleted uranium, for storage and transportation. When taking a “shot,” the source is wound out to the target location through a guide tube that terminates at a collimator that is configured to direct the gamma rays only towards the object to be examined.

Iridium-192 has a relatively short half-life of 73.8 days, which means that the source material has effectively decayed away after about two years. The functional lifetime of each iridium-192 radiography source—when the source has decayed so much that exposure time increases so much that it becomes cost effective to change out the source—is about 6-8 months. Disused iridium-192 sources are either returned to the device supplier for disposal as low-level waste after five or more years decay or are stored by licensees pending disposal.

Figure 8.4 (Ir-192 radiography disk sources, with a pencil for size reference)



Gamma Radiography – Selenium-75

Selenium-75 is another radioisotope which can be used for industrial radiography. It has similar radiological traits to iridium-192, with a half-life of about 120 days. Selenium-75 decays exclusively through electron capture with gamma ray energies varying from 66-401 keV, having an average energy of about 215 keV and a decay product that is stable arsenic. The longer half-life also gives it a longer useful lifetime than iridium-192 sources, but its lower energy gamma emissions relative to iridium-192 means that it is ideal to radiograph thinner or lower density substrates. Selenium-75 sources are much less common than iridium-192 sources for radiography in the United States and were not included in the primary for isotopes identified by the National Academies Report.⁴⁴³

Selenium-75 sources require less shielding than iridium-192 due to its lower energy so the units built specifically for selenium-75 are slightly lighter at around 42 pounds, although some cameras can accept either isotope. They are also handheld and portable.

Gamma Radiography – Cobalt-60

Another radioisotope used in gamma radiography is cobalt-60. Cobalt-60 has a 5.27-year half-life undergoing beta decays and releasing two gamma rays of 1173 and 1332 keV, averaging 1250 keV. The progeny is stable nickel-60. Cobalt-60 radiography units require significant shielding to protect users and the environment from the more energetic gamma emission compared with either iridium-192 or selenium-75 sources. As a result, the device is significantly heavier, with a starting weight over 700 pounds. Cobalt-60 radiography units are less portable than the iridium and selenium units and require carts or heavy machinery to move. However, due to the higher energy gamma emissions, they are used to examine thicker materials.

⁴⁴³ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008).

Cobalt-60 cameras tend to be used for large structures such as buildings and bridges; their use is less common in remote field environments (i.e., pipelines). These devices typically contain 60 Ci to 300 Ci when new and exceed the 8.10 Ci Category 2 threshold throughout their service lives.

Gamma Radiography – Ytterbium-169

Ytterbium-169 is occasionally used for gamma radiography. It has a 32-day half-life decaying via electron capture, emitting a range of gamma rays from 63-308 keV, averaging about 120 keV. The decay product is stable thulium-169. In contrast to the other radiography sources, Yb-169 is used only for thinner metals, typically under 1.5 centimeters thick. The low gamma energies allow for smaller exclusion areas during its use compared with other radiography sources, reducing the impact on productivity. However, it is not useful for larger metal thicknesses.

Non-isotopic Testing and Analysis Methods - X-ray

A common analysis method which works on the same physical principles as gamma radiography, but without radioisotopes is x-ray radiography. As previously mentioned, x-ray and gamma radiography are historically interchangeable and are technologically similar. It is even common to say to “x-ray” an object even when the source emits gamma rays. The difference between the technologies is the source of the high energy photons. Electrical x-ray machines do not use radioisotopes to produce ionizing radiation and instead use x-ray tubes or linacs to produce ionizing radiation on-demand with electricity by accelerating electrons onto a tungsten (or other heavy metal) target. In the laboratory or other controlled setting, x-ray radiography generally provides superior image quality compared with gamma radiography. However, x-ray systems require an active and reliable power source to function both the x-ray units and the remote power batteries are more sensitive to extreme environments. The power supply requirements for x-ray devices may preclude them from use in some industrial environments, such as remote locations or extreme temperatures. X-ray radiography uses film exposure to capture an image of the target structure/material. Similar to gamma radiography, the image is then developed and assessed in a non-field location by personnel trained to do so.

The energy of the x-rays produced will vary based on the technology and application. Often times, these machines are heavy, and voluminous to accommodate for the shielding requirements, and are often fixed in place to accommodate a specific process need. However, some x-ray units may also be manufactured as portable units making them suitable for field locations, such as pipelines, similar to the isotopic radiography described earlier. Historically these units typically were based on medical applications and provided x-rays up to 120-150 kV, which is not sufficient to penetrate many metals found in industrial field environments. Instead portable x-ray units are used on thinner materials in the field.

Modern x-ray tubes can be manufactured up to 400-450 kV, and generate x-rays and bremsstrahlung energy averaging about one third of the e-beam voltage. A betatron or linac can be used to produce x-ray and bremsstrahlung energies into the low MeV range. X-ray units which produced 200 keV photons are typically much larger than the iridium and selenium counterparts and also less portable. However, progress has been made with x-ray pipeline crawlers or similar devices.⁴⁴⁴ These devices use a portable power source and x-ray generator to travel through a pipeline taking radiography measurements along the way. These units are

⁴⁴⁴ Simon, et al., A Novel X-Ray Tool for True Sourceless Density Logging, *Petrophysics* Vol. 59, NO. 5, October 2018, 565-587.

typically quite long—about 2 meters—and can only be used in relatively straight portions of pipe because their length makes it difficult to navigate tight turns.⁴⁴⁵

X-ray radiography may require setting up a radiation exclusion zone during uses to prevent unnecessary worker exposure to radiation. These zones have the potential to interrupt work functions. Unlike gamma radiography, there would not be additional safety/security considerations during storage and transport.

Similar to gamma radiography, x-ray radiography requires little surface preparation prior to inspection of the material.⁴⁴⁶ The devices require more training to operate than a gamma radiography source but provide similar data to gamma radiography that is equally easy to interpret. The technology devices take seconds to minutes to capture data, but it may take more time to view the results depending on x-ray capture techniques (digital vs. film). It has higher resolution than other NDE techniques; however, it cannot be used to measure residual wall thickness and is subject to linear delamination. It can, however, be used to examine both solid materials and matrix materials such as concrete.

Ultrasonic

Ultrasonic testing (UT) is a common and effective industrial tool for finding defects in materials and welds. For this method, a high-frequency sound wave is sent through a transducer and propagated through the material of interest. As the acoustical waves pass through the material, they may be reflected (echoed) by the free end of the material; defects and larger pores; or a differing medium. The echoes can be captured by a receiver, which may be collocated with the transducer. A trained operator can use the results of this scan against a standard to determine whether sonic discontinuities exist in the material.

It is not always possible to send or receive sound waves directly through a probe into the material, so a couplant gel is frequently applied to the surface of the material to aid in transmitting the sound waves. It is a consumable component of UT testing, but cannot be used in all remote operating environments and does not work well in very cold conditions.

UT requires an active power system to collect and interpret data. The results are collected in real time but require a skilled technician to interpret. Reflected signals can often have ambiguous sources and findings, and identifying flaws is dependent on the operator.

An operational advantage of UT is that it can generally be applied without significant facility disruption. No radiation exclusion zone is required. The absence of additional safety/security considerations is also an advantage compared with gamma radiography.

Technology Purchase and Replacement Considerations

The following section outlines considerations potential buyers would base their purchase or replacement decisions on, including device ability to meet site and application requirements, cost, and security factors of each technology.

⁴⁴⁵ Shilton, Mark, International Source Supplies and Producers Association (ISSPA), “Gamma Radiography,” presentation to the Alternative Technology Working Group, May 2017.

⁴⁴⁶ Shilton, Mark, International Source Supplies and Producers Association (ISSPA), “Gamma Radiography,” presentation to the Alternative Technology Working Group, May 2017.

Lifecycle Technology Costs

The costs of gamma radiography devices will vary depending on the source and needs of the users. It is difficult to obtain prices for a public report, but the NAS found that “portable pulsed x-ray radiography systems begin at approximately \$50,000” or more.⁴⁴⁷ The maintenance and operations costs for these systems are low but do include radiological safety and security costs.

NAS found that portable accelerator-based x-ray systems “begin more in the range of \$200,000. Ultrasonic systems typically range from \$50,000 to \$100,000,”⁴⁴⁸ though the cost may have changed since the report was issued. The maintenance and operational costs of these alternatives are higher than those of gamma radiography systems. The x-ray-based systems are also subject to radiation-protection protocols.

Device Ability to Meet Site and Application Requirements

This chapter presented a variety of alternative technologies to gamma radiography NDT. However, there are still certain operational considerations and environments that would preclude widespread adoption or use of those alternatives.

Gamma radiography is most often used in remote field locations without ready access to reliable power and is subject to exposure to weather and temperature extremes. It may also be used in place that are difficult to access, either because they are spatially limited or high above a surface that would preclude the use of more voluminous or heavy equipment. Viable replacement technologies will need to be able to perform well in these environments.

Comparison of Gamma Radiography and X-ray Techniques to Ultrasonic Testing

Unlike radiography, UT only requires access to one side of a material to search for defects; however, the transducer must be able to physically access the material to be interrogated. UT can be used to detect defects below the surface because it travels completely through the materials and can be reflected by the defect. However, shallow surface defects may be hidden from the operator due to the use of couplant, which may fill such defects. Because of the direction of the acoustical waves, UT is very capable of finding laminar delamination in a material and of measuring the residual wall thickness of the material. UT works best when examining a solid material; it is less effective with matrix materials such as concrete. While the technique can be used to detect large pores, it is not particularly effective at identifying the location or nature of those pores. Smaller pores may be missed entirely if they are much smaller than the wavelength of the sonic signal. UT is also weak at detecting defects parallel to the propagation of the sound wave. While UT can detect most defects in a controlled laboratory setting, a direct comparison does not account for difficult locations or environments that affect the technique in many real-life situations.⁴⁴⁹

A study was conducted to look at the ability for radiography and UT to find defects are a range of conditions.⁴⁵⁰ It found that radiography was capable of finding flaws in slag carbon steel piping for depth

⁴⁴⁷ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008).

⁴⁴⁸ Committee on Radiation Source Use and Replacement, National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008).

⁴⁴⁹ Moran, T.L., et al., *Applying Ultrasonic Testing in Lieu of Radiography for Volumetric Examination of Carbon Steel Piping*, United States Nuclear Regulatory Commission (USNRC), Office of Nuclear Regulatory Research, NUREG/CR-7204; May 2015, <https://www.nrc.gov/docs/ML1525/ML15253A674.pdf>.

⁴⁵⁰ Roux, Izak J., “Is it Ultrasonic or is it Radiography inspection?” M Eng. (SA) RAE Engineering & Inspection Ltd. Paper delivered at the 2005 National Pressure Equipment Conference, (Alberta, Canada: Banff, February 2005).

from 1.2 – 52.3 millimeters, but ultrasonic had difficulty finding those defects in flaws in depths under 6.2 millimeters, it was especially disadvantaged when trying to find those defects when only scanning one side of the pipe. Radiography could find pores at thicknesses from 0.3 millimeters and above whereas UT could not. But UT was superior at finding lack of fusion weld defects when both sides of the pipe were detected as compared with radiography which rarely detected those defects.

Both radiography and UT may be used to find defects; however, each technique has its advantages and disadvantages owing to how the interrogative wave (high-energy photon or sound) interacts with the medium and reflects or passes through defects. The figure located on the next page shows when each technique is strong or weak against a given defect. Orientation of the interrogative method is important: Radiography should find defects that are aligned in the same direction or oblique to the radiation path, but it may be weak when searching for defects perpendicular to the path. UT, on the other hand, should find defects that are perpendicular or oblique to the sound wave but may miss defects oriented in the direction of the wave. Radiography and UT would usually have different orientations relative to the surface for similar inspections.

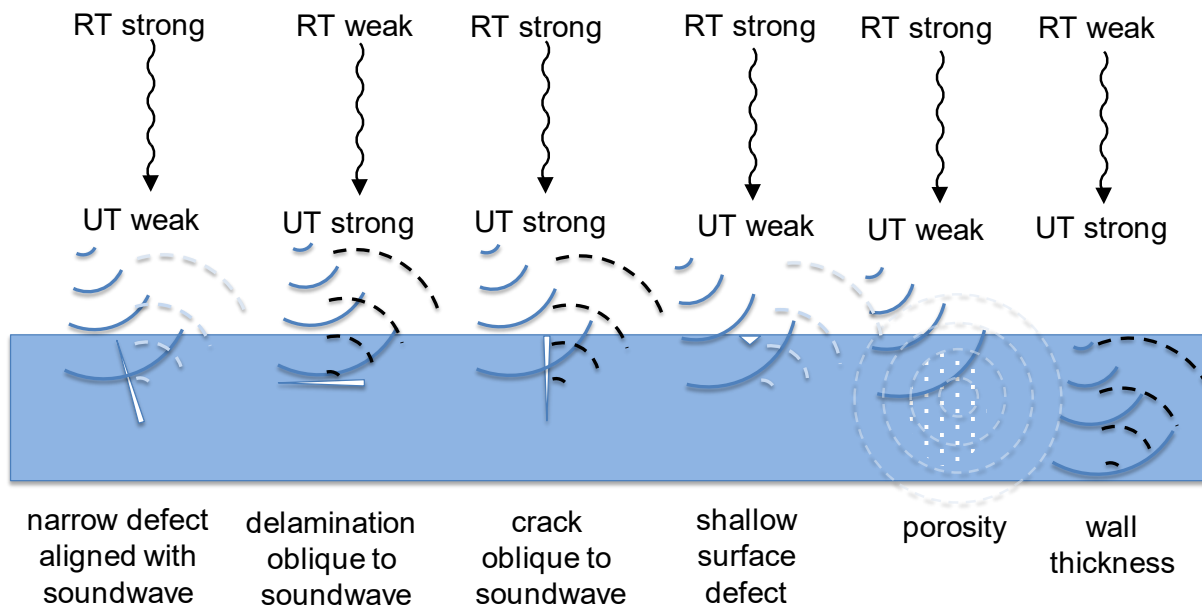
Radiography does not use a couplant so it should spot surface defects; UT may miss surface defects because of the use of couplants that can propagate the sound wave. Radiography is effective at determining differences in density and can spot pores, whereas UT may not detect pores if they do not reflect. However, UT will reflect off surface boundaries and can be used to determine material thickness; radiography is less capable of making these measurements.

The figure below provides a summary of the advantages and disadvantages of each technique as described in this chapter. A key takeaway from the figure and study is that UT and radiography have competing strengths and weaknesses; for this reason, they should not be thought of as competing NDT methods, but rather as complimentary. The risk of missing a possible unacceptable defect is lowered by employing both techniques.

UT - RT Comparison

UT measures sonic discontinuities

RT measures mass/density



UT / RT – Comparison

Pro

UT

- Measures residual wall thickness
- Linear defects normal to the sound beam are well detected (delamination)
- There is no radiation safety hazard
- Instantaneous real-time results
- Requires access to only one side of a pipe
- Automatable (PAUT, AUT)

RT

- Lower level technician training needed
- Minimal surface preparation
- Works at low temperature
- Sources may be easier to project to highly inaccessible places
- Simple interpretation of data – not technician dependent
- No calibration standards are needed
- Generally less expensive than UT
- Generally faster than UT
- Generally higher resolution than UT

Con

UT

- Requires higher level technician training
- Requires surface preparation / sonic coupling
- Does not work at very low temperature
- Less sensitive to detecting porosity
- Transducers may not be locatable in highly inaccessible places
- Interpretation of data is technician dependent
- Calibration standards are needed

RT

- Doesn't Measure residual wall thickness
- Linear defects normal to the radiation beam may go undetected (delamination)
- Requires access to both sides of a pipe
- Radiation safety hazard / security risk
- Delayed results
- Regulatory / transportation constraints
- RT Staff criminal background checks

Administrative and Regulatory Costs

This section describes the administrative and regulatory aspects associated with NDT and radiography.

Regulatory Controls

The use of gamma radiography is subject to numerous regulations for operation, storage, and transportation. Many of these regulations are well-established. In fact, the original 10 C.F.R. Part 20, developed in the 1950s, was exclusive to safety and security for radiography. The transport of portable systems is regulated by the NRC under 10 C.F.R. Parts 20, 34, 37, and 71⁴⁵¹ and by DOT under 49 C.F.R. Parts 100-185.⁴⁵²

Radiography sources must meet the special form requirements outlined in 10 C.F.R. 71.75,⁴⁵³ including: (1) the radionuclide source must be contained in a solid piece or a sealed capsule that can only be opened by destroying the capsule; (2) at least one dimension of the capsule must not be less than 5 millimeters; and (3) the source must satisfy the specific requirements of 49 C.F.R. 173.469⁴⁵⁴ that the source capsule does not break, melt, or leak after being subjected to a series of prescribed impact, deformation, leaching, and high-temperature exposure tests.⁴⁵⁵

Device Competency: Education, Training, Certification, Standards

There are numerous professional society codes governing the use of NDT methods including gamma radiography and x-ray techniques. The most pertinent and extensive is the ASME Boiler and Pressure Vessel Code.⁴⁵⁶ The American Petroleum Institute (API) also produces codes on the manufacture of oil and gas steel pipelines, assembly, and inspection.⁴⁵⁷ These codes will specify appropriate inspections for the project that will be contracted by the owner or responsible party to an NDT provider.

There are specific requirements to be a certified radiographer. In order for NRC and Agreement States to consider someone a radiographer, and thus allow them to be designated as such on a license, States and NRC have adopted regulations requiring industrial radiographers to attend a radiation safety course, complete a specified number of on-the-job training hours, and successfully complete a written examination prior to being certified. In order to facilitate the certification of industrial radiographers, 10 states as well as the American Society for Nondestructive Testing (ASNT) have nationally recognized certification programs, with documented experience and education requirements. Certification programs must comply with 10 C.F.R. § 34 “Licenses for Industrial Radiography and Radiation Safety Requirements for Industrial Radiographic Operations.”⁴⁵⁸

Certifications for other types of nondestructive testing is also through ASNT⁴⁵⁹. While some NDT practitioners achieve certification in a variety of techniques, many will specialize in a chosen field and will tend to tend take contracts that require those already known techniques. This may present a long-term obstacle to

⁴⁵¹ Standards for Protection Against Radiation, 10 C.F.R. Part 20; Packaging and Transportation of Radioactive Material, 10 C.F.R. Part 71; Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material, 10 C.F.R. Part 37.

⁴⁵² Transportation, 49 C.F.R. § 100 – 185.

⁴⁵³ Qualification of Special Form Radioactive Material, 10 C.F.R. § 71.75.

⁴⁵⁴ Tests for Special Form Class 7 (Radioactive) Materials), 49 C.F.R. § 173.469.

⁴⁵⁵ National Research Council, *Radiation Source Use and Replacement: Abbreviated Version*, Washington, DC: The National Academies Press, 2008.

⁴⁵⁶ American Society of Mechanical Engineers (ASME), Committee on Nondestructive Examination, *ASME Boiler and Pressure Vessel Code: Nondestructive Examination*, ASME, 2017.

⁴⁵⁷ Energy American Petroleum Institute (API), “Standards,” Accessed December 3, 2018, www.api.org/Standards.

⁴⁵⁸ Licenses for Industrial Radiography and Radiation Safety Requirements for Industrial Radiographic Operations, 10 C.F.R. § 34.

⁴⁵⁹ The American Society for Nondestructive Testing (ASNT), “Certification,” Accessed December 3, 2018, www.asnt.org/MajorSiteSections/Certification.

replacing gamma radiography sources with alternative technologies in applicable work environments. Since technicians may default to institutional legacy methods rather than look for certifications and new techniques outside their area of expertise.

Disposal Costs and Considerations for Sealed Source Radiography Devices

The proper disposal of radioactive materials used by the private sector is the responsibility of the licensees who benefit from them commercially. As most gamma radiography sources have a short half-life and limited initial activity levels, neither commercial disposal access, nor commercial disposal costs are typically constraining issues for the use or end-of-life management these sources (excluding cobalt-60).

Appendix 1: Blood Irradiation Devices with FDA 510(k) Classification Status

Through the FDA's 510(k) clearance or premarket notification device regulation and guidance procedure for medical devices, it established a process for premarket submissions to grant substantial equivalence to another legally United States-marketed device. To gain equivalence, premarket devices must meet several conditions, including a demonstration that a device with different technological characteristics does not “raise new questions of safety and effectiveness” and is “at least as safe and effective as the legally marketed device.” If all conditions are met, the device will receive a 510(k) clearance or premarket notification. This process does not require clinical studies for approval.

Noted: This table is from a 2012 report, and not all devices may currently be commercially available and/or serviced by their original companies. Non-isotopic irradiators have been shaded in the table.

Table A.1: List of Blood Irradiation Devices with 510(k) Clearance and Indications for Use (courtesy of FDA⁴⁶⁰)

Cleared Blood Irradiators 510(K) number	Product name Manufacturer	Radiation Source	Predicate Device	Intended Use or Indications for Use (from Product Literature)
K837346	Not available	Cs-137	Preamendments	Not available
K851828	IBL-437-C Syncor Intl. Corp.	Cs-137	Preamendments	Not available
K865027	IBL-137C Cis-us Inc.	Cs-137	K851828	The IBL-137C has been devised to provide blood banks and medical laboratories with an uncomplicated autonomous irradiation unit intended specifically for biological and medical applications as well as blood products.
K915766	Model 109 JL Shepherd and Assoc.	Co-60	Cis-US (K851828), Gammacell 1000 (K837346), and IBL-137C (K865027)	To irradiate blood products with Co-60 gamma radiation to reduce the risk of GVHD by delivering approximately 2500 cGy to blood and cellular components prior to transfusion into fetuses, immunoincompetent or immunocompromised patients, donor units known to be from first degree relatives.
K915767	Model 143 Series Blood Product Irradiators JL Shepherd and Assoc.	Cs-137	Cis-US (K851828), Gammacell 1000 (K837346), and IBL-137C (K865027)	The model 143 series blood product irradiation facilities are designed to deliver a designated dose of gamma radiation to blood and blood products. This gamma radiation inactivates leukocytes with the intention of preventing GVHD.

⁴⁶⁰ U.S. Food and Drug Administration (FDA), Radiological Devices Advisory Panel, Blood Irradiators—Unclassified: Executive Summary, April 12, 2012, <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/RadiologicalDevicesPanel/UCM299255.pdf>.

Cleared Blood Irradiators 510(K) number	Product name Manufacturer	Radiation Source	Predicate Device	Intended Use or Indications for Use (from Product Literature)
K952291	Gammacell 3000 ELAN Best Theratronics Ltd.I	Cs-137	Gammacell -1000	Irradiation of blood, blood components and biologicals to inactivate leucocytes/lymphocytes.
K963497	Gammacell 3000 ELAN Version 1.0 and Gammacell 1000 ELITE Version 1.0 Best Theratronics Ltd.	Co-60/Cs-137	K952291	Irradiation of blood and blood components to inactivate leukocytes and lymphocytes.
K974210	RS 3000 Shielded X-ray Radiation Source Rad-Source, Inc.	X-ray	K865027 IBL 437C	Irradiation of blood or blood products packaged in transfusion bags in accordance with “Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products” (July 22, 1993) when irradiation to reduce the risk of GVHD is indicated.
K032684	Raycell Best Theratronics Ltd.	X-ray	K974210 RS 3000	Intended for the irradiation of blood and blood products packaged in transfusion bags when irradiation to reduce the risk of GVHD is indicated and is used in accordance with “Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products” (July 22, 1993).
K050963	Gammacell 1000 Elite and Gammacell 3000 Elan Best Theratronics Ltd.I	Cs-137	K963497	To irradiate cellular blood products to inactivate T-lymphocytes in order to prevent GVHD.
K051065	Raycell X-ray Blood Irradiator Best Theratronics Ltd.	X-ray	K032684	The Raycell X-ray Blood Irradiator is intended for use in the irradiation of blood and blood products (packaged in transfusion bags) to inactivate T-lymphocytes for the prevention of GVHD according to applicable FDA, AABB, Health Canada and European guidelines. The Raycell X-ray Blood Irradiator is also intended for use in the irradiation of intra-operatively salvaged blood for cancer patients undergoing surgery to assist in the prevention of metastasis.
K082921	RS 3400 Rad Source X-ray Blood Irradiator Rad Source Technologies, Inc.	X-ray	RS 3000 (K974210)	The 3400 Rad Source X-ray blood irradiator is intended for the irradiation of blood or blood products packaged in transfusion bags in accordance with “Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products” (July 22, 1993) when irradiation to reduce the risk of GVHD is indicated.

Appendix 2: Lifecycle Cost Estimates for Cesium and X-Ray Irradiators

The following tables include an estimated range of installation, variable, fixed, and termination costs for both cesium irradiators and x-ray irradiators over the life of the device. The estimates are taken directly from the 2013 [Cost-Benefit Analysis of Switching from Cesium-Chloride to X-ray Blood Irradiators](#) study, conducted at the request of the NNSA.⁴⁶¹

The study completed a lifecycle analysis of costs associated with a cesium-137 blood irradiator and an x-ray blood irradiator. Researchers compiled cost data through a comprehensive literature review, personal interviews, and less than 10 specific license data submissions from the 2013 American Association of Physicists in Medicine (AAPM) survey, and performed statistical analysis on the data to estimate possible cost ranges with a lower and upper bound for each of the given categories. In addition, the point price estimate represents an assumed sample statistic, based on the anticipated distribution of the cost range. All lifecycle costs were calculated at net present value (in 2013), which accommodates the different lifespan of the cesium-137 and x-ray devices. Important costs include resources invested in the installation of a new device, annual fixed costs that occur regardless of the irradiator throughput, annual variable costs that are affected by irradiator throughput, and termination costs that are incurred at the end of the lifetime of an irradiator.

The analytical methodology used with the report accounts for any statistical uncertainty in the cost amounts; however, actual site costs may vary greatly—either higher or lower—depending on a multitude of site-specific factors. The estimates can inform the industry’s broad understanding of device costs and benefits, but should not be used to inform individual investment decisions. Readers should refer to the original study to clarify the definition of terms used or the study methodology.

⁴⁶¹ Bakken, Erik, Katie Cary, Allison Derrick, Ellen Hildebrand, Kyle Schroeckenthaler, and Malika Taalbi, “Cost-Benefit Analysis of Switching from Cesium-Chloride to X-ray Blood Irradiators,” (University of Wisconsin-Madison, 2013).

Table A.2: Installation Costs (United States dollars)

Component (Unit)	Low Range Price Estimate	High Range Price Estimate	Point Price Estimate
Cesium Irradiator Purchase Price: (Total Dollars)	160,000	325,000	242,500
X-Ray Purchase Price: (Total Dollars)	160,000	240,000	220,000
Cesium Site Preparation: (Total Dollars)	5,000	10,000	7,500
X-Ray Site Preparation: (Total Dollars)	0	50,000	18,600
Cesium Initial Legal/Licensing/RSO/Public Health Costs: (Total Dollars)	4,000	20,000	15,400
X-Ray Initial Legal/Licensing/RSO/Public Health Time Costs: (Total Dollars)	2,000	3,000	2,500
Cesium Initial Fingerprinting/Background Check Costs: (Total Dollars)	2,000	5,000	3,800
Cesium Installation/Setup/Commissioning/Shielding Design Considerations: (Total Dollars)	30,000	38,000	34,000
Cesium Transportation of Device (Total Dollars)	3,000	50,000	28,800
X-Ray Transportation of Device	0	2,600	2,000
Cesium Import Permit- Cesium Only (Total Dollars)	7,000	7,000	7,000
Cesium Global Threat Reduction Initiative Security ⁴⁶² Equipment/Installation (Total Dollars)	317,800	500,000	404,800

⁴⁶² This initiative is a voluntary, government-funded program.

Table A.3: Fixed Costs (United States dollars)

Component (Unit)	Low Range Price Estimate	High Range Price Estimate	Point Price Estimate
Cesium Security Infrastructure Maintenance: (Annual Total Dollars)	1,000	8,600	4,900
Cesium Security Background Check: (Annual Total Dollars)	2,400	2,400	2,400
Cesium Anticipated Security Ongoing Costs: (Annual Total Dollars)	4,000	7,500	5,800
Cesium Service Contract/Warranty: (Annual Total Dollars)	1,000	14,000	6,000
X-Ray Service Contract/Warranty: (Annual Total Dollars)	2,000	17,000	8,500
X-Ray Year 7 Power Supply Upgrade: (Total Dollars)	5,000	5,000	5,000
X-Ray Year 10 Power Supply Upgrade: (Total Dollars)	10,000	10,000	10,000
Cesium Regulation Personnel: (Annual Salaries in Dollars) ⁴⁶³	57,500	57,500	57,500
Cesium Regulation Licensing: (Annual Total Dollars)	650	8,700	4,700
X-Ray Regulation Licensing: (Annual Total Dollars)	3,000	8,700	5,900
Nuclear Regulatory Commission Costs Not Covered by Licensing: (Annual Total Dollars)	4,600	4,600	4,600

⁴⁶³ For further explanation, see page 10 of: Bakken, Erik, Katie Cary, Allison Derrick, Ellen Hildebrand, Kyle Schroeckenthaler, and Malika Taalbi, "Cost-Benefit Analysis of Switching from Cesium-Chloride to X-ray Blood Irradiators," (University of Wisconsin-Madison, 2013).

Table A.4: Variable Costs (United States dollars)

Component (Unit)	Low Range Price Estimate	High Range Price Estimate	Point Price Estimate
Cesium Blood Units Per Site Per Day: (Average Daily Blood Units Irradiated)	0	50	25
X-Ray Blood Units Per Site Per Day: (Average Daily Blood Units Irradiated)	0	50	25
Cesium Blood Unites Per Batch: (Average Blood Unites Irradiated Per Run)	1	4	2.5
X-Ray Blood Unites Per Batch: (Average Blood Units Irradiated Per Run)	5	5	5
Cesium Wage of Technician/Operator: (Hourly Blood Units Irradiated Per Run)	27	37	29
X-Ray Wage of Technician/Operator (Hourly Wage in United States Dollars)	27	37	29
Cesium Irradiation Time Per Batch: (Run Time in Minutes Per Batch)	1.7	8.6	5
X-Ray Irradiation Time Per Batch: (Run Time in Minutes Per Batch)	5	5	5
Base Price of Electricity: (Dollars Per Kilowatt Hours)	0.076	0.1647	.1081
Cesium Kilowatts of Electricity Consumed: (Kilowatts Consumed Per Minute of Run-Time)	0.3	0.3	0.3
X-Ray Kilowatts of Electricity Consumed: (Kilowatts Consumed Per Minute of Run-Time)	2	2	2
X-Ray Parts Replacement: (Average Annual Dollars)	10,000	10,000	10,000
Cesium Costs of Downtime: (Average Annual Dollars)	2,300	2,300	2,300
X-Ray Costs of Downtime: (Average Annual Dollars)	4,000	4,000	4,000

Table A.5: Termination Costs (United States dollars)

Component (Unit)	Low Range Price Estimate	High Range Price Estimate	Point Price Estimate
Cesium Physical Costs of Disposal: (Total Dollars)	75,000	150,000	-----
X-Ray Physical Costs of Disposal: (Total Dollars)	0	2,600	1,300
Cesium Site to Vendor Disposal Fee: (Total Dollars)	15,000	40,000	-----
Cesium Site to Off-Site Recovery Project Disposal Fee: (Total Dollars)	0	190,000	-----
Off-Site Recovery Project Costs Not Covered by Fees: (Total Dollars)	75,000	920,000	-----

Appendix 3: Glossary

These terms and definitions were taken from the National Research Council *Radiation Source Use and Replacement: Abbreviated Version* study.

Absorbed dose: The quantity of ionizing radiation deposited into a material, including an organ or tissue, expressed in terms of the energy absorbed per unit mass of material. The basic unit of absorbed dose is the rad or its SI equivalent, the gray (Gy).

Accelerator: A device that accelerates charged subatomic particles; also called a particle accelerator. In the context of this report, these devices are used to generate energetic beams of electrons that can be directed at an object to be irradiated or at a tungsten, tantalum, or gold target, which converts the electron energy into x-rays that irradiate an object.

Actinide: Any of a series of chemically similar radioactive elements with atomic numbers ranging from 89 (actinium) through 103 (lawrencium). This group includes uranium (atomic number 92), plutonium (atomic number 94), and americium (atomic number 95).

Activity: The rate of decay of a radionuclide; more formally, the number of decays per unit time. Its SI unit is the becquerel (Bq), corresponding to one radioactive decay (disintegration) per second; its old unit, the curie (Ci), was originally defined as the activity of 1 gram of radium-226 or 3.7×10^{10} disintegrations per second.

Becquerel (Bq): A unit of measure for activity. One becquerel is one disintegration (radioactive decay) per second. A gigabecquerel (GBq) is 10⁹ Bq (1 billion becquerels) and a terabecquerel (TBq) is 1,012 Bq (1 million million becquerels).

Bremsstrahlung: Radiation emitted by the slowing down of light charged particles, such as the x rays produced when electrons from an accelerator are stopped in a metal target.

Category 1 source: A radiation source that, if not managed safely or securely, could lead to the

death or permanent injury of individuals in a short period of time.

Category 2 source: A radiation source that, if not managed safely or securely, could lead to the death or permanent injury of individuals who may be in close proximity to the radioactive source for a longer period of time than for Category 1 sources.

Curie (Ci): A unit of measure for activity equal to 3.7×10^{10} (37 billion) disintegrations (radioactive decays) per second.

Decay product: A resultant particle from a radioactive disintegration.

Effective dose: The equivalent dose averaged across all organs that accounts for the varying sensitivity of different organs and tissues to the biological effects of ionizing radiation. The effective dose has the same units as the equivalent dose.

Equivalent dose: The absorbed dose averaged across the organ or tissue of interest multiplied by a radiation-weighting factor, w_R , to account for the differences in biological detriment (harm) to an organ that result from differences in radiation type and energy for the same physical dose received by the organ. The SI unit of equivalent dose is sievert (Sv); the old unit is the rem. For x rays, gamma rays, and electrons, w_R is 1; for protons, it is 5, for alpha particles, 20; and for neutrons, it ranges from 5 to 20 depending on neutron energy.

Exposure: A metric based on the ability of photons to ionize air. Its old unit, roentgen (R), is defined as a charge of 2.58×10^{-4} C produced per kilogram of air. The SI unit of exposure is 2.58×10^{-4} C per kilogram of air.

External exposure: An exposure received from a source of ionizing radiation outside of the body (NCRP, 2001).

External cost: A cost from an action or economic transaction that is not included in the monetary cost of the activity or transaction and therefore is borne by parties not directly involved in the transaction.

Fission: The splitting of a nucleus into at least two fragments, accompanied by the release of neutrons and energy. Fission may be initiated by absorption of a neutron or, in some materials such as californium-252, can happen spontaneously.

Fusion: The joining together of two or more nuclei. The most commonly used fusion reaction is the deuterium-tritium reaction, also called the D-T reaction.

Gamma ray: High-energy electromagnetic radiation. In this report, radiation emitted by decay of a radionuclide is always referred to as gamma radiation to distinguish it from radiation from an x-ray generator.

Graft-versus-host-disease (GvHD): A rare but usually fatal complication of transfusion in which functional donor immune cells (T lymphocytes) attack the recipient's tissues and the recipient's immune system is unable to eliminate the donor lymphocytes.

Greater-than-Class-C waste: Radioactive waste that contains concentrations of certain radionuclides above the Class C limits in 10 C.F.R. § 61.55.

Half-life: The time during which one half of a given quantity of a radionuclide undergoes radioactive decay.

Hazard: A potential source of a negative consequence or harm.

High-Z material: See atomic number.

Hydrocarbon: In the context of this report, oil or natural gas.

Irradiation: Exposure to radiation.

Ionizing radiation: Radiation that is sufficiently energetic to ionize the matter (i.e., remove electrons from the atoms) through which it moves.

Natural background radiation: Radiation that exists naturally in the environment. It includes cosmic and solar radiation, radiation from radioactive materials present in rocks and soil, and radioactivity that is inhaled or ingested.

Nondestructive testing (NDT): Testing that does not destroy the object under examination.

Panoramic irradiator: An irradiation device that does not have shielding built into the device. In such devices, the sources must be housed in thick, shielded structures.

Radiation dose: The quantity of radiation energy deposited in an object or medium divided by the mass of the object or medium. The radiation dose of interest in this report is ionizing radiation. Ionizing radiation doses can be expressed as absorbed doses, equivalent doses, or effective doses. Its SI unit, gray (Gy), is defined as 1 joule (J) of energy absorbed per kilogram of absorbing medium; its old unit is the rad, defined as 100 erg of energy absorbed per gram of absorbing medium.

Radiation dose rate: The quantity of ionizing radiation absorbed by a medium per unit mass of the medium per unit time.

Radiation exposure: The act of being exposed to radiation. Also referred to as irradiation. Formally in radiation detection and measurement, radiation exposure is related to the ability of photons to ionize air.

Radiation source: Radioactive material packaged to use the radiation it emits.

Radioactive: Elements that are unstable and transform spontaneously (i.e., decay) through the emission of ionizing radiation, a process known as radioactive decay.

Radiography: The use of radiation to create images of a subject, especially the internal

features of a subject. Medical radiography is familiar from routine dental examinations. Industrial radiography is a form of nondestructive testing for aircraft wings, pipes, turbines, reinforced concrete construction, and other applications.

Radioisotope: An atom with an unstable nucleus, which undergoes radioactive decay.

Radiotherapy: Treatment of disease with ionizing radiation.

Radiosurgery: Focal irradiation techniques that use multiple, non-coplanar radiation beams to deliver a prescribed dose of radiation to lesions, primarily in the brain.

Safety: In the context of this report, concerning prevention of failure, damage, human error, and other inadvertent acts involving radiation sources that could result in accidental radiation exposures.

Safety risks: In the context of this report, risks that arise from exposures of people to radiation as a direct result of accidents involving radiation sources.

Security: In the context of this report, concerning protection against theft, sabotage, and other malevolent acts involving radiation sources.

SI: International System of Units (from the French *Système International d'Unités*), also sometimes referred to as the metric system.

Solubility: The ability of a substance to dissolve in water or, more generally, in a solvent.

Transuranic waste: Radioactive waste containing long-lived radioactive transuranic elements (elements with atomic numbers greater than 92) such as plutonium in concentrations greater than 100 nanocuries per gram.

Ultrasonics: The use of high-intensity acoustic energy for materials examination.

Vitrification: A process for immobilizing radioactive material in glass matrixes.

Well logging: The practice of measuring the properties of the geologic strata through which a well has been drilled and recording the results as a function of depth.

X-ray: High-energy electromagnetic radiation. In this report, radiation emitted by a machine such as an x-ray tube or an electron accelerator with a high-Z target is always referred to as x-ray radiation to distinguish it from radiation from decay of a radionuclide.

Appendix 4: References

- 10 C.F.R. § 37, “Physical Protection of Byproduct Material” [NRC 2013f].
- 21 C.F.R. § 117 “Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food.”
- Akkurt, Ridvan, et al., “Towards Everyday-NMR: An Operator’s Perspective,” *Petrophysics*, 2009, 50 (6): 495-510, SPWLA-2010-v51n3a1.
- American Association of Physicists in Medicine (AAPM), “2013-10-17 AAPM Irradiator Survey—Final,” presentation to the Nuclear Alternate Technology Working Group, April 7, 2015.
- American Society of Mechanical Engineers (ASME), Committee on Nondestructive Examination, *ASME Boiler and Pressure Vessel Code: Nondestructive Examination*, ASME, 2017.
- ANSI/AAMI/ISO 11135:2014, Sterilization of Health Care Products - Ethylene oxide - Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices and ANSI/AAMI/ISO 10993-7 Biological Evaluation of Medical Devices, Part 7: Ethylene Oxide Sterilization Residuals. ANSI/AAMI/ISO 20857:2010, Sterilization Of Health Care Products - Dry Heat - Requirements for the Development, Validation and Routine Control of a Sterilization Process for Medical Devices and ANSI/AAMI/ISO 17665-1:2006/(R)2013, Sterilization of Health Care Products - Moist Heat - Part 1: Requirements for the Development, Validation, and Control of a Sterilization Process for Medical Devices.
- ANSI/AAMI/ISO 11137-1:2006/(R)2010, Sterilization of Health Care Products - Radiation - Part 1: Requirements for Development, Validation, and Routine Control of a Sterilization Process for Medical Devices [Including: Amendment 1 (2013)], ANSI/AAMI/ISO 11137-2:2013, Sterilization of Health Care Products - Radiation - Part 2: Establishing the Sterilization Dose, and ANSI/AAMI/ISO 11137-3:2006/(R)2010, Sterilization of Health Care Products - Radiation - Part 3: Guidance on Dosimetric Aspects.
- ANSI/AAMI/ISO TIR13004:2013, Sterilization of health care products — Radiation —Substantiation of a Selected Sterilization Dose.
- Atun, Rifat, et al., “Expanding Global Access to Radiotherapy” *The Lancet Oncology Commission* 2015, 16: 1153-86.
- Badruzzaman, A. et al., *Radioactive Sources in Petroleum Industry: Applications, Concerns and Alternatives*, SPE 123593, Presented at SPE Asia Pacific Health, Safety, Security, and Environment Conference and Exhibition, August 4-5, 2009.
- Badruzzaman, A., et al., “Neutron Generators as Alternatives to Am-Be Neutron Sources in Well Logging: An Assessment of Fundamentals,” *Petrophysics*, Vol. 60, No.1, pages 136-170, 2019.
- Badruzzaman, Ahmed, “An Assessment of Fundamentals of Nuclear-based Alternatives to Conventional Chemical Source Bulk Density Measurement,” *Petrophysics*, 55 (2014) 5, 415-434.
- Badruzzaman, Ahmed, et al, Scoping Study on Developing Alternatives to Radionuclide-based Logging Technologies, LLNL-TR-679101, October 30, 2015.
- Bakken, Erik, Katie Cary, Allison Derrick, Ellen Hildebrand, Kyle Schroeckenthaler, and Malika Taalbi, “Cost-Benefit Analysis of Switching from Cesium-Chloride to X-ray Blood Irradiators,” (University of Wisconsin-Madison, 2013).
- Bakri, A., K. Mehta and D. R. Lance,” Sterilizing Insects with Ionizing Radiation” V. A. Dyck, J. Hendrichs, and A.S. Robinson, Eds., *Sterile Insect Technique: Principles and Practice in Area-Wide Integrated Pest Management*, IAEA; Springer (2005), 236.
- Barclay, Hugh John, “Determination of the sterile release rate for stopping growing age-structured populations,” *International Journal of Pest Management* 62 (2015) 40–54.
- Barkai-Golan, Rivka and Peter A. Follett, Irradiation for Quality Improvement, Microbial Safety and Phytosanitation of Fresh Produce, Academic Press/Elsevier (2017).
- Borchardt, R.W., “Strategy for the Security and Use of Cesium-137 Chloride Sources,” Advisory Committee on the Medical Uses of Isotopes (ACMUI) CsCl Irradiator Subcommittee, November 24, 2008, Available at http://hps.org/govtrelations/documents/nrc_cscl_options_secy08-0184.pdf.

Brown, David, "The Truth About Radiation Processing: 'Niche Markets... Hidden Gems'" Mevex Corporation, presented at the 2017 Texas A&M Electron Beam Workshop.

Brown, Tony, "Mevex Equipment for Phytosanitary Irradiation," Mevex Corporation, presentation delivered at Chapman University, 2016, <https://www.chapman.edu/scst/files/news-and-events/phytosanitation-irradiation-16/brown.pdf>.

BT GB100-80 and Equinox are 15,000 Ci and 390 cGy/min. "Technical Specifications," Best Theratronics, Accessed march 21, 2019, http://www.theratronics.ca/PDFs/BT_GB_100-80_tech_specs.pdf.

Busch-Petersen, E and A Kafu, "Assessment of quality control parameters during mass rearing of a pupal colour genetic sexing strain of the Mediterranean fruit fly," *Entomologia Experimentalis et Applicata* 51 (1989) 241–248.

Cancino, J, L Ruiz, J Perez, and E Harris. "Irradiation of *Anastrepha ludens* (Diptera: Tephritidae) eggs for the rearing of the fruit fly parasitoids, *Fopius arisanus* and *Diachasmimorpha longicaudata* (Hymenoptera: Braconidae)," *Biocontrol Science and Technology* 19 (2009) S1, 167–177.

Cancino, Jorge, Lía Ruíz, Mariana Viscarret, John Sivinski and Jorge Hendrichs, "Application of Nuclear Techniques to Improve the Mass Production and Management of Fruit Fly Parasitoids," *Insects* 3 (2012) 1105-1125, doi:10.3390/insects3041105.

Cleland, M.R., "Industrial applications of electron accelerators," CAS 2005 - CERN Accelerator School: Small Accelerators, Proceedings. 10.5170/CERN-2006-012.383, (2006), <https://cds.cern.ch/record/1005393/files/p383.pdf>.

Codex Alimentarius, "General Standard for Irradiated Foods," Codex Stan 106-1983, Rev. 1-2003.

Codex Alimentarius, Code of Practice for Radiation Processing of Food (CAC/RCP 19-1979).

Cokragan, Ahmet, "Commercial Use of Phytosanitary Irradiation," MEVEX presentation Toluca, Mexico, October 14, 2015.

"Company," Stellararray, accessed August 16, 2016, <http://stellar-ray.com/>.

Cooke Jr., Claude E., "Radial Differential Temperature (RDT) Logging - A New Tool for Detecting and Treating Flow Behind Casing," SPE-7558-PA, *J Pet Technol*, 1979, 31 (6): 676-682.

"Cyberknife Locations," CyberKnife, accessed January 27, 2017, <https://cyberknife.com/locations>.

Department of Energy (DOE), "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; DOE 2016), available at <https://www.energy.gov/em/waste-management/waste-and-materials-disposition-information/greater-class-c-low-level>.

Department of Health and Human Services (HHS), The 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey Report, 2015, page 63.

Dethier, Philippe, Industrial & Sterilization Solutions (IBA), "Industrial Gamma and X-ray: 'Same but Different,'" Whitepaper, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

Dineley, Jude, "MR-guided cobalt-60 system measures up," *Medical Physics Web*, 2015.

Elekta Corporate, "Why MR/RT?" Website, accessed May 3, 2018, <https://www.elekta.com/>.

Ellis, Darwin V and Julian M. Singer, *Well Logging for Earth Scientists*, Second Edition, Springer, New York, 2007.

Emergo Group, "How long it takes the USFDA to clear medical devices via the 510(k) process: An examination of 15,000 medical device applications cleared by the U.S. Food and Drug Administration between 2012 and 2016," Emergo Publication, March 2017, <https://www.emergogroup.com/resources>.

Energy American Petroleum Institute (API), "Standards," Accessed December 3, 2018, www.api.org/Standards.

Energy Policy Act of 2005. Pub. L. 109-58, Sec. 170H.f. August 8, 2005.

Enkerlin, WR, A Bakri, C Caceres, JP Cayol, A Dyck, U Feldmann, et al. "Insect pest intervention using the sterile insect technique: Current status on research and on operational programs in the world," Research Institute for Subtropics, Naha; Japan (2003) 11–24.

Evans, M., et al., *A sourceless alternative to conventional LWD nuclear logging*, SPE 62982, in Proc. SPE Annual Technical Conference and Exhibition, Dallas, TX, October 3-4, 2000.

FAO / IAEA Division of Nuclear Techniques in Food and Agriculture, "Development of Electron Beam and X-Ray

Applications for Food Irradiation,” CRP Code: D61024, CRP ID: 2082.

Federal Trade Commission v. Steris Corporation, No. 1:15 CV 1080, 2015 WL 5657294, (N.D. Ohio, September 24, 2015).

Final Rule,” 9 C.F.R. § 304, et al., Federal Register, Vol. 61, No. 144, Thursday, July 25, 1996, 38805-38989.

Fisher, K., “Genetic sexing strains of Mediterranean fruit fly (Diptera: Tephritidae).

Follett, P.A. and E.D. Weinert, “Phytosanitary irradiation of fresh tropical commodities in Hawaii: Generic treatments, commercial adoption, and current issues,” *Radiation Physics and Chemistry* 81 (2012) 1064–1067.

Follett, Peter A. and Lisa G. Neven, “Current trends in Quarantine Entomology,” *Annual Review of Entomology*, Vol. 51: 359 (2006).

Follett, Peter “Phytosanitary Irradiation for Fresh Horticultural Commodities: Generic Treatments, Current Issues, and Next Steps,” *Stewart Postharvest Review*, 3:1 (2014).

Follett, Peter, “Entomology and the Evolution of Generic Doses.” Presentation, Eighth Annual Phytosanitary Irradiation Forum, June13-15, 2018.

Fox, Christopher H., Edwin Romeijn, Bart Lynch, Chunhua Men, Dionne M Aleman, and James F Dempsey, “Comparative Analysis of Co Intensity-Modulated Radiation Therapy,” *Phys. Med. Biol.* 2008, 53: 3175-3188.

Frost & Sullivan, “2012 Medical Devices Outlook: Setting the Stage for What’s Next,” April 28, 2016.

Galford et al., A new neutron-induced gamma ray spectroscopy tool for geochemical logging, SPWLA 50th Annual Logging Symposium, Paper X, 2009.

Galloway, Rick, Industrial & Sterilization Solutions (IBA), “X-ray: The emerging alternative to gamma irradiation,” Texas A&M University Hands-On Workshop in E-Beam Irradiation Technologies, (2017).

Gamma Industry Processing Alliance (GIPA) and International Irradiation Association (iia), “A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products,” (November 2017), <http://iiaglobal.com/wp-content/uploads/2018/01/White-Paper-Comparison-Gamma-Eb-Xray-and-EO-for-Sterilisation.pdf>.

Gamma Industry Processing Alliance (GIPA), “Cobalt-60 Irradiation and Alternative Technologies,” Presentation to the Alternative Technology Working Group (2015)

Gamma Industry Processing Alliance (GIPA), “Comparison of Cobalt-60 and X-Ray Technologies,” GIPA Fact Sheet., 2007, http://gipalliance.net/wp-content/uploads/documents/GIPAFactsheet_XrayComparison_000.pdf.

Garrison, Lance, Arden Dougan, and Allen Bakel, “Research and Development to Enable the Replacement of Radioisotope Sources,” *Proceedings of the Institute for Nuclear Materials Management* (2016).

Gibson, Brian W. et al., “Comparison of Cesium-137 and X-ray Irradiators by Using Bone Marrow Transplant Reconstitution in C57BL/6J Mice,” *Comparative Medicine*, Vol. 65, No. 3, June 2015, pages 165–172.

Gilchrist, Allen, et al., *Nuclear Source Replacement-Promises and Pitfalls*, SPWLA-2011-KKK, Presented at the 51st Annual Symposium of the Soc. of Petrophysicists and Well Log Analysts, May 14-18, 2011.

Gisela C., C. Mendes, MD, Teresa R. S. Brandao, PhD, and Cristina L. M. Silva, PhD, “Ethylene oxide sterilization of medical devices: A review,” *Am J Infect Control*, November 2007, Vol. 35, I. 9, Pages 574–581.

Griffiths, Alison, Luke Marinovich, Michael B. Barton, and Sarah J. Lord, “Cost analysis of Gamma Knife stereotactic radiosurgery,” *International Journal of Technology Assessment in Health Care*, 2007, 23(4): 488-494.

Guy J. Hallman and Carl M. Blackburn, “Phytosanitary Irradiation,” *Foods*, 2016, 5, 8; doi:10.3390/foods5010008.

Guy J. Hallman, “Process Control in Phytosanitary Irradiation of Fresh Fruits and Vegetables as a Model for Other Phytosanitary Treatment Processes,” *Food Control* (2016).

Hallman, Guy J. and Carl M. Blackburn, “Phytosanitary Irradiation,” *Foods*, Vol. 5(1): 8 (2016).

Hallman, Guy J. and Paisan Loaharanu, “Phytosanitary Irradiation – Development and Application,” *Journal of Radiation Physics and Chemistry, Radiat. Phys. Chem* (2016).

Hallman, Guy J., "Control Of Stored Product Pests By Ionizing Radiation," *Journal of Stored Products Research*, 52 (2013).

Hallman, Guy J., "Phytosanitary Applications of Irradiation," *Comprehensive Reviews in Food Science and Food Safety*, Vol.10 (2011).

Hallman, Guy J., "Phytosanitary Measures to Prevent the Introduction of Invasive Species," *Ecological Studies*, Vol. 193 (2007).

Hallman, Guy J., "Process Control in Phytosanitary Irradiation of Fresh Fruits and Vegetables as a Model for Other Phytosanitary Treatment Processes," *Food Control*, (2016).

Hallman, Guy J., Yves M. Hénon, Andrew G. Parker, and Carl M. Blackburn, "Phytosanitary irradiation: An overview," 2016 — *Florida Entomologist* — Volume 99, Special Issue 2 (2016).

Hallman, Guy J., "Process Control in Phytosanitary Irradiation of Fresh Fruits and Vegetables as a Model for Other Phytosanitary Treatment Processes," *Food Control* (2016).

Hayes, Inc, "510(k) vs. PMA: Do you know the difference?" Hayes Evidence Blog, December 21, 2016, <https://www.tractmanager.com/blog/510k-vs-pma-do-you-know-the-difference/>.

Henon 2015 presentation (IAEA).

Herron, S.L. and M.H. Herron, *Quantitative Lithology: An application for Open- and Cased-hole Spectroscopy*, Trans, SPWLA 37th Annual Logging Symposium, Paper E, 1996.

Hogstrom, Kenneth and Peter Almond. 2006. "Review of Electron Beam Therapy Physics." *Phys. Med. Biol.* 51: R455-R489.

H. R. 5515, "John S. McCain National Defense Authorization Act for Fiscal Year 2019," Public Law No: 115-232, August 13, 2018, <https://www.congress.gov/bill/115th-congress/house-bill/5515>.

Hoisak, Jeremy D. P., Todd Pawlicki, Gwe-Ya Kim, Richard Fletcher, and Kevin L. Moore, "Improving linear accelerator service response with a real-time electronic event reporting system," *Journal of Applied Clinical Medical Physics*, 2014, 15(5): 4807.

IAEA, "Development of New Applications of Machine Generated Food Irradiation Technologies: Report of a Consultant Meeting on a Proposed Coordination Research Project", IAEA Headquarters, Vienna, Austria 26-30 May 2014 (2015), page 4.

IBA, "Review of Radiation Sterilization Technologies for Medical Devices," Whitepaper, 2013, <http://www.iba-industrial.com/downloads/sterilization-of-medical-devices/17>.

ICF Incorporated, "Cost-Benefit Analysis for Potential Alternative Technologies for Category 1 and 2 Radioactive Sources," U.S. Nuclear Regulatory Commission, Contract No. NRC-02-05-002, Task Order No. 5 (2009).

Industrial & Sterilization Solutions (IBA), "Ahead of the curve," IBA Whitepaper, 2014, page 1, www.iba-industrial.com/downloads/sterilization-of-medical-devices/17.

Industrial & Sterilization Solutions (IBA), "Review of Radiation Sterilization Technologies for Medical Devices" (2013).

Industrial & Sterilization Solutions (IBA), Practical Advantages of the Rhodotron, Whitepaper, <http://www.iba-industrial.com/downloads/sterilization-of-medical-devices/17>.

Interagency Working Group on Alternatives to High-Activity Radioactive Sources, Transitioning from High-Activity Radioactive Sources to Non-Radioisotopic (Alternative) Technologies A Best Practices Guide for Federal Agencies, (Washington, DC, 2016). https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/ndrd-gars_best_practices_guide_final.pdf.

International Atomic Energy Agency (IAEA), "International Database on Insect Disinfestation and Sterilization (IDIDAS), Accessed November 27, 2018, [https://nucleus.iaea.org/sites/naipc/ididas/SitePages/International%20Database%20on%20Insect%20Disinfestation%20and%20Sterilization%20\(IDIDAS\).aspx](https://nucleus.iaea.org/sites/naipc/ididas/SitePages/International%20Database%20on%20Insect%20Disinfestation%20and%20Sterilization%20(IDIDAS).aspx).

International Atomic Energy Agency (IAEA), "Trends in Radiation Sterilization of Health Care Products," (Vienna: IAEA, 2008).

International Atomic Energy Agency (IAEA), "Manual of Good Practice in Food Irradiation," Technical Reports Series No. 481 (2015).

International Atomic Energy Agency (IAEA), "Radiation Protection in Radiotherapy, Part 7: Design of Facilities and Shielding, Lecture 2: Shielding," IAEA Training Material on Radiation Protection in Radiotherapy, accessed January 27, 2017.

International Atomic Energy Agency (IAEA), "Thematic Plan for the Development and Application of the Sterile Insect Technique (SIT) and Related Genetic and

Biological Control Methods for Disease Transmitting Mosquitoes,” IAEA TC project INT0089 - Developing Human Resources and Supporting Nuclear

International Atomic Energy Agency (IAEA), IAEA Human Health Report No. 10: Radiotherapy Facilities: Master Planning and Concept Design Considerations, (Vienna: International Atomic Energy Agency: 2014).

International Irradiation Association (IIA), “Industrial Radiation with Electron Beams and X-rays,” Rev. 6 (May 2011).

International Isotopes Inc., “2017 Securities and Exchange Commission Form 10-K Annual Report,” filed March 30, 2018, page F-19.

International Plant Protection Convention (IPPC), “International standards for phytosanitary measures,” Food and Agriculture Organization of the United Nations, ISSN 2521-7232.

IOTRON, “The IOTRON Electron Beam Experience,” Texas A&M E-Beam Workshop (2017).

ISO/ASTM 51900 Guide for Dosimetry in Radiation Research on Food and Agricultural Products,” International organization for Standardization (ISO), 2nd edition, June 2009, <https://www.iso.org/standard/44182.html>.

Jeffers, Laura A., “Commodity Approval & Irradiation as a Phytosanitary Treatment,” USDA-APHIS Presentation, Texas A&M E-Beam Workshop, (2017).

Johnson, Judy A. Spencer S. Walse and James S. Gerik, “Status of Alternatives for Methyl Bromide in the United States,” *Outlooks on Pest Management*, April 2012, DOI: 10.1564/23apr02.

Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, “Sterile Insect Technique,” accessed October 3, 2018, <http://www-naweb.iaea.org/nafa/ipc/sterile-insect-technique.html>.

King III, G., et al., “Density Logging Using An Electron Linear Accelerator as the X-Ray Source,” *Nuclear Instruments and Methods in Physics Research* B24/25, 990-994, 1987.

Klassen, W., “Area-wide integrated pest management and the sterile insect technique,” V. A. Dyck, J. Hendrichs, and A.S. Robinson, Eds., *Sterile Insect Technique: Principles and Practice in Area-Wide Integrated Pest Management*, IAEA; Springer (2005) 39.

Kopolovic, I., et al., “A systematic review of transfusion-associated graft-versus-host disease,” *Blood*, 2015, 126(3):406-414.

Kroc, Thomas K., Jayakar C. T. Thangaraj, Richard T. Penning, and Robert D. Kephart, “Accelerator-Driven Medical Sterilization to Replace Co-60 Sources,” Fermi National Accelerator Laboratory, July 6, 2017.

Lambert, Byron J., Todd A. Mendelson, and Michael D. Craven, “Radiation and Ethylene Oxide Terminal Sterilization Experiences with Drug Eluting Stent Products,” AAPS PharmSciTech, December 2011, Vol. 12, No. 4, DOI: 10.1208/s12249-011-9644-8.

Leitman, Susan F, “Role of Cesium-137 Chloride Irradiators in Transfusion Medicine,” Nuclear Alternate Technology Working Group (Washington, DC: April 7, 2015).

Libai Xu, et al., “A Comprehensive Investigation of Source Effects on Neutron Porosity Response for Logging-While-Drilling Measurements,” *Petrophysics*, 51 (2010) 3: 185-198.

Licenses for Industrial Radiography and Radiation Safety Requirements for Industrial Radiographic Operations, 10 C.F.R. § 34.

M. Evans et al., *A sourceless alternative to conventional LWD nuclear logging*, SPE 62982, in Proc. SPE Annual Technical Conference and Exhibition, Dallas, TX, October 3-4, 2000.

MacKenzie, C. and K. Smith, “University of California System-Wide Plan to Replace Caesium Irradiators With Alternative Technologies,” paper presented at the IAEA International Conference on the Security of Radioactive Material: The Way Forward for Prevention and Detection, 3-7 December 2018, Vienna, Austria IAEA-CN-269.

Markets and Markets Research, “Sterilization Equipment Market: By Type, Product, End User & By Region – Forecast to 2021,” (September 2016).

Massaro, Gino, E-beam and X-ray Technologies: innovative solutions, IBA Presentation, March 5, 2015, [http://iiaglobal.com/uploads/documents/S2.35%20Massaro%20\(IBA\)%20.pptx](http://iiaglobal.com/uploads/documents/S2.35%20Massaro%20(IBA)%20.pptx).

Maxim Integrated, “Sterilization Methods and Their Impact on Medical Devices Containing Electronics,” Application Note 5068, <https://www.maximintegrated.com/en/app-notes/index.mvp/id/5068>.

McCullough, J., Goldfinger, D., Gorlin, J., Riley, W. J., Sandhu, H., Stowell, C., Ward, D., Clay, M., Pulkrabek,

S., Chrebtow, V. and Stassinopoulos, A., “Cost implications of implementation of pathogen-inactivated platelets,” *Transfusion*, 2015, 55: 2312–2320. doi:10.1111/trf.13149.

Medicare Payment Advisory Commission (MEDPAC), *Report to the Congress: Medicare and the Health Care Delivery System*, (Washington, DC: Medicare Payment Advisory Commission, June 2017).

Mehta, K and A Parker, “Characterization and dosimetry of a practical x-ray alternative to self-shielded gamma irradiators,” *Radiation Physics and Chemistry* 80 (2011) 107–113.

Mendes, Gisela C. C., Teresa R. S. Brandao, and Cristina L. M. Silva, “Ethylene oxide sterilization of medical devices: A review,” *Am J Infect Control*, November 2007, Volume 35, Issue 9, Pages 574–581.

Moran, T.L., et al., *Applying Ultrasonic Testing in Lieu of Radiography for Volumetric Examination of Carbon Steel Piping*, United States Nuclear Regulatory Commission (USNRC), Office of Nuclear Regulatory Research, NUREG/CR-7204; May 2015, <https://www.nrc.gov/docs/ML1525/ML15253A674.pdf>

Mount Sinai, “Mount Sinai Experience in Migrating From Radioactive Irradiators to x-Ray Irradiators for Blood and Medical Research Applications,” New York, September 2018, https://media.nti.org/documents/Mt._Sinai_Final_Report.pdf.

National Institutes of Health, Office of Infrastructure Research, “Shared Instrumentation Awards,” accessed August 26, 2016, https://dpcpsi.nih.gov/orip/diic/fy_sig_awards.

National Research Council National Academies, “Acute Exposure Guideline Levels for Selected Airborne Chemicals,” Volume 9 (2010).

National Research Council, *Radiation Source Use and Replacement: Abbreviated Version* (Washington, DC: National Academies Press, 2008).

Nicole Reichel et al., Neutron-Gamma Density (NGD): Principles, Field Test Results and Log Quality Control of a Radioisotope-free Bulk Density Measurement, Paper GGG, Proc. SPWLA 53rd Annual Symposium, Cartagena, Colombia, June 16-20, 2012.

Nordion Inc. Fiscal 2013 Annual Report, page 15.

NRC, Industrial Radiography Licensee Toolkit, <https://www.nrc.gov/materials/miau/industrial-uses/rad-toolkit.html>.

Nuclear Alternate Technologies Working Group, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, September 12, 2018.

Nuclear Regulatory Commission (NRC), “Strategy for the Security and Use of Cesium-137 Chloride Sources,” SECY-08-0184, November 24, 2008, page 8.

Ontario Energy Board, Province of Ontario, Canada, “Ontario’s Long Term Energy Plan 2017: Delivering Fairness and Choice,” <https://www.ontario.ca/document/2017-long-term-energy-plan>.

Optimizing high temperature treatment of mass-reared temperature-sensitive lethal strains,” *Journal of Economic Entomology* 91 (1998) 1406–1414.

Page, Brandi R., Alana D. Hudson, Derek W. Brown, Adam C. Shulman, May Abdel-Wahab, Brandon J. Fisher, and Shilpen Patel, “Cobalt, Linac, or Other: What Is the Best Solution for Radiation Therapy in Developing Countries?” *International Journal of Radiation Oncology, Biology, Physics* 2014, 89(3): 476–480.

Parker, A. and K. Mehta, “Sterile insect technique: A model for dose optimization for improved sterile insect quality,” *Florida Entomologist* 90 (2007) 88–95.

Parker, Andrew, “Sterile Insect Technique: Irradiators for SIT,” for the Nuclear Alternate Technologies Working Group, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, September 12, 2018.

Pemper, R., et al, 2006, *A New Pulsed Neutron Sonde for Derivation of Formation Lithology and Mineralogy*, SPE 102770, Proc. SPE Annual Technical Conference and Exhibition, September 24-27, 2006.

Philippe Dethier, Industrial & Sterilization Solutions (IBA), “Industrial Gamma and X-ray: ‘Same but Different,’” Whitepaper, page 10, April 2016, http://iiaglobal.com/uploads/documents/IBA.white_paper_-_x-ray_vs_gamma.pdf.

Philippe Dethier, MEVEX, “Megawatt Sterilization Systems,” presentation to the April 2019 International Meeting on Radiation Processing (IMRP) in Strasbourg, France.

Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material, 10 C.F.R. § 37.

Pillai, Suresh and C. Bogran, “Ionizing Irradiation for Phytosanitary Applications and Fresh Produce Safety,” *Global Safety of Fresh Produce: A Handbook of Best*

Practice: Innovative Commercial Solutions and Case Studies, Woodhead Publishing (2014).

Pillai, Suresh and Shima Shayanfar, "Electron Beam Technology and Other Irradiation Technology Applications in the Food Industry," in Topical Collection "Applications of Radiation Chemistry" Top Curr Chem (Z) (2017) 375:6; DOI 10.1007/s41061-016-0093-4.

Pillai, Suresh, "Principles of Ionizing Radiation and eBeam and X-ray Dose Deposition," Texas A&M University, (2017).

Pillai, Suresh, "Justification for Irradiation Technologies," Texas A&M University, (2017).

Podgorsak, E.B. "Chapter 5: Treatment Machines for External Beam Radiotherapy," presentation based on the IAEA publication Radiation Oncology Physics: A Handbook for Teachers and Students by E.B. Podgorsak, (ISBN 92-0-107304-6), Version 2012.

Podgorsak, E.B., *Radiation Oncology Physics: A Handbook for Teachers and Students*, (Vienna: International Atomic Energy Agency: 2005).

"Premarket Notification 510(k)," U.S. Food and Drug Administration, last updated September, 16, 2015, <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/>.

Qualification of Special Form Radioactive Material, 10 C.F.R. § 71.75.

Radiation Source Protection and Security Task Force, Nuclear Regulatory Commission, *The 2010 Radiation Source Protection and Security Task Force Report*, (Washington, DC: 2010), page 4, Available at <http://www.nrc.gov/security/byproduct/2010-task-force-report.pdf>.

Radiation Source Protection and Security Task Force, Nuclear Regulatory Commission, *The 2014 Radiation Source Protection and Security Task*.

Radtke, RJ et al., *A Capture and Inelastic Spectroscopy Tool Takes Geochemical Logging to Next Level*, Proc. 53rd SPWLA Annual Symposium, Cartagena, Columbia, June 16-20, 2012.

Ravichandran, R., "Has the time come for doing away with Cobalt-60 teletherapy for cancer treatments?" *Journal of Medical Physics*, 2009, 34(2): 63-65, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2805891/>.

Regan, Donna and Miriam A. Markowitz, American Association of Blood Banks, "Changes to the 30th edition of *Standards for Blood Banks and Transfusion*

Services," Association Bulletin #16-05 to AABB Members, March 17, 2016.

Roux, Izak J., "Is it Ultrasonic or is it Radiography inspection?" M Eng. (SA) RAE Engineering & Inspection Ltd. Paper delivered at the 2005 National Pressure Equipment Conference, (Alberta, Canada: Banff, February 2005).

Sandgren, P. and B. Diedrich, "Pathogen inactivation of double-dose buffy-coat platelet concentrates photochemically treated with amotosalen and UVA light: preservation of in vitro function," 2015, *Vox Sang* 108(4): 340-349.

Sarwar, M, N Ahmad, A Rashid, and SMM Shah, "Valuation of gamma irradiation for proficient production of parasitoids (Hymenoptera: Chalcididae & Eucilidae) in the management of the peach fruit-fly, *Bactrocera zonata* (Saunders)," *International Journal of Pest Management* 61 (2015) 126–134.

Schlesinger, David, "Historical and Technical Overview of Gamma Knife Radiosurgery," AAPM Summer School (Burlington, VT), 2014, <https://www.aapm.org/meetings/2014SS/documents/SU05SchlesingerFINALforHandouts.pdf>.

Scott, B. R., K. M. Gott, and J. Wilder, "A Comparison of In Vivo Cellular Responses to Cs-137 Gamma Rays and 320-Kv X Rays," *Dose-Response*, 11: 444–459, 2013.

SelectUSA, "Medical Technology Spotlight," U.S. Department of Commerce, accessed March 28, 2018.

Shayanfar, S., K. Mena and S.D. Pillai, "Quantifying the Reduction in Potential Health Risks from Non O157 Shiga Toxin Producing Escherichia Coli in Strawberries by Electron Beam Processing," *Food Control*, 72: 324-327 (2017).

Shilton, Mark, International Source Supplies and Producers Association (ISSPA), "Gamma Radiography," presentation to the Alternative Technology Working Group, May 2017.

Shilton, Mark, representing International Source Supplies and Producers Association (ISSPA), "Gamma Radiography," presentation to the Alternative Technology Working Group, May 2017.

Simon, Matthew, et al., "A Novel X-Ray Tool for True Sourceless Density Logging," *Petrophysics*, Vol. 50, No. 5, October 2018.

Sotera Health, "Nordion Acquires Technology to Expand Future Global Cobalt-60 Supply,"

<https://www.nordion.com/nordion-acquires-technology-to-expand-future-global-cobalt-60-supply/>.

Standards for Protection Against Radiation, 10 C.F.R. § 20.

Steri-Tek, website, 2018, <https://steri-tek.com/>.

“Sterilization of health-care products—Ethylene oxide—Requirements for the development, validation and routine control of a sterilization process for medical devices,” International organization for Standardization (ISO), 1st edition, May 1, 2007.

Sugden, S., “Relative Economics and Practicalities of Gamma and X-ray Sterilization,” Panel on Gamma and Electron Irradiation, 2016 Gamma Industry Processing Alliance (GIPA), “Comparison of Cobalt-60 and X-Ray Technologies,” GIPA Fact Sheet, 2014.

Sugranes, Jorge, “Basic Operating Principles and Validation of Electron Beam Irradiation Systems,” *Journal of Validation Technology*, November 2005.

T.L. Moran, et al., *Applying Ultrasonic Testing in Lieu of Radiography for Volumetric Examination of Carbon Steel Piping*, United States Nuclear Regulatory Commission (USNRC), Office of Nuclear Regulatory Research, NUREG/CR-7204; May 2015, Available at <https://www.nrc.gov/docs/ML1525/ML15253A674.pdf>.

Texas Administrative Code, Title 30, Part 1, Chapter 336, Texas Commission on Environmental Quality, Radioactive Substance Rules, Subchapter N, “Fees for Low-Level Radioactive Waste Disposal.”

The American Society for Nondestructive Testing (ASNT), “Certification,” Accessed December 3, 2018, www.asnt.org/MajorSiteSections/Certification.

University of Vermont Department of Surgery, “Orthovoltage vs. megavoltage x-rays,” accessed January 27, 2017.

U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), “FDA APHIS Approved Treatment Facilities,” August 5, 2018, https://www.aphis.usda.gov/import_export/plants/manuals/ports/downloads/national_treatment_facility_lis_t.pdf.

U.S. Department of Agriculture Food Safety and Inspection Service, “Pathogen Reduction; Hazard Analysis and Critical Control Point (HACCP) Systems.

U.S. Department of Agriculture: Animal and Plant Health Inspection Service, “CPHST: Treatment Technology,” webpage accessed March 28, 2017.

U.S. Department of Energy (DOE)/U.S. Nuclear Regulatory Commission (NRC) Working Group, Radiological Dispersal Devices: An Initial Study to Identify Radioactive Materials of Greatest Concern and Approaches to Their Tracking, Tagging, and Disposition, U.S. Department of Energy and U.S. Nuclear Regulatory Commission, May 2003. Available at <http://energy.gov/sites/prod/files/edg/media/RDDRPTF14MAYa.pdf>

U.S. Department of Health and Human Services (HHS), “Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion: Draft Guidance for Industry,” March 2016, <http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM425952.pdf>.

U.S. Energy Information Administration (EIA), Form EIA-23L, Annual Survey of Domestic Oil and Gas Reserves, 2013.

U.S. Food and Drug Administration (FDA), “Deciding When to Submit a 510(k) for a Change to an Existing Device,” Final Guidance, issued on October 25, 2017.

U.S. Food and Drug Administration (FDA), “Hazard Analysis and Risk-Based Preventive Controls for Human Food: Guidance for Industry,” Draft Guidance, January 18, 2018.

U.S. Food and Drug Administration (FDA), Radiological Devices Advisory Panel, Blood Irradiators – Unclassified: Executive Summary, (2012).

U.S. Food and Drug Administration (FDA), “Report on FDA’s Policy to be Proposed Regarding Premarket Notification Requirements for Modifications to Legally Marketed Devices,” Report to Congress, January 7, 2014.

U.S. Food and Drug Administration (FDA), “Risk Profile: Pathogens and Filth in Spices,” Center for Food Safety and Applied Nutrition, 2017.

U.S. Food and Drug Administration (FDA), “Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile: Guidance for Industry and Food and Drug Administration Staff,” issued on January 21, 2016.

U.S. Food and Drug Administration (FDA), “The New 510(k) Paradigm Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications,” Final Guidance, issued March 20, 1998.

U.S. Food and Drug Administration (FDA), “The 510(k) Program: Evaluating Substantial Equivalence in

Premarket Notifications [510(k)]: Guidance for Industry and Food and Drug Administration Staff,” July 28, 2014, Available at www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM284443.pdf.

U.S. Food and Drug Administration (FDA), “Updated FDA Risk Profile: Pathogens and Filth in Spices (2017),” February 2018 released, <https://www.fda.gov/downloads/Food/FoodScienceResearch/RiskSafetyAssessment/UCM581362.pdf>.

U.S. Food and Drug Administration (FDA), *Radiological Devices Advisory Panel, Blood Irradiators—Unclassified: Executive Summary*, April 12, 2012.

U.S. Food and Drug Administration (FDA), Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion Transmission of Zika Virus, February 2016, accessed June 29, 2016, available at <https://www.govinfo.gov/content/pkg/FR-2016-02-19/pdf/2016-03393.pdf>.

U.S. Nuclear Regulatory Commission (NRC), “Branch Technical Position on Concentration Averaging and Encapsulation,” last updated October 26, 2016, <https://www.nrc.gov/waste/llw-disposal/llw-pa/llw-btp.html>.

U.S. Nuclear Regulatory Commission (NRC), Cost-Benefit Analysis for Potential Alternative Technologies for Category 1 and 2 Radioactive Sources, by ICF Incorporated, L.L.C., (Rockville, MD: 2009), page 36.

U.S. Nuclear Regulatory Commission (NRC), “Industrial Radiography Licensee Toolkit,” last updated July 7, 2017, <https://www.nrc.gov/materials/miau/industrial-uses/rad-toolkit.html>.

U.S. Nuclear Regulatory Commission (NRC), “Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material (10 C.F.R. § 37),” December 2015 (Washington DC).

U.S. Nuclear Regulatory Commission (NRC), “Regulatory Analysis for Final Rule: Physical Protection of Byproduct Material, (10 C.F.R. §§ 20, 30, 32, 33, 34, 35, 36, 37, 39, 51, 71, and 73),” (Washington, DC: December 2011).

U.S. Nuclear Regulatory Commission (NRC), “Rulemaking Issue Affirmation: Final Rule: Physical

Protection of Byproduct Material (10 C.F.R. §§ 20, 30, 32, 33, 34, 35, 36, 37, 39, 51, 71, and 73),” (Washington D.C., December 2011, <http://www.nrc.gov/reading-rm/doc-collections/commission/secys/2011/2011-0170scy.pdf>.

Valant-Spaight et al, “Field Examples with a Slim LWD Density/Neutron Instrument Containing a Californium-252 Neutron Source and Three Neutron Detectors,” Proc. 47th SPWLA Annual Logging Symposium, Paper CCC.

ViewRay, Inc., Form 10-K Annual Report, Securities and Exchange Commission, filed March 17, 2017, <http://phx.corporate-ir.net/phoenix.zhtml?c=253882&p=irol-sec>.

W.D. Flanagan et al., *A New Generation Nuclear Logging System*, Paper Y, Transactions, SPWLA 32nd Annual Logging Symposium, Midland, Texas, June 16-19, 1991.

Whitaker, Barbee, Srijana Rajbhandary, and Andrea Harris, *The 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey Report*, AABB, December 18, 2015, page 63, Available at <https://www.aabb.org/research/hemovigilance/bloodsurvey/Documents/2013-AABB-Blood-Survey-Report.pdf>.

World Institute of Nuclear Security, “Alternative Technologies to Radioactive Sources,” Workshop Report, Brussels, October 8-9, 2013; American Association of Physicists in Medicine (AAPM), “2013-10-17 AAPM Irradiator Survey—Final,” presentation to the Nuclear Alternate Technology Working Group, April 7, 2015.

World Nuclear Association, “Radioisotopes in Medicine,” accessed January 2019, <https://www.world-nuclear.org/information-library/non-power-nuclear-applications/radioisotopes-research/radioisotopes-in-medicine.aspx>.

Xu, Libai, et al., “A Comprehensive Investigation of Source Effects on Neutron Porosity Response for Logging-While-Drilling Measurements,” *Petrophysics*, 51 (2010) 3: 185-198.