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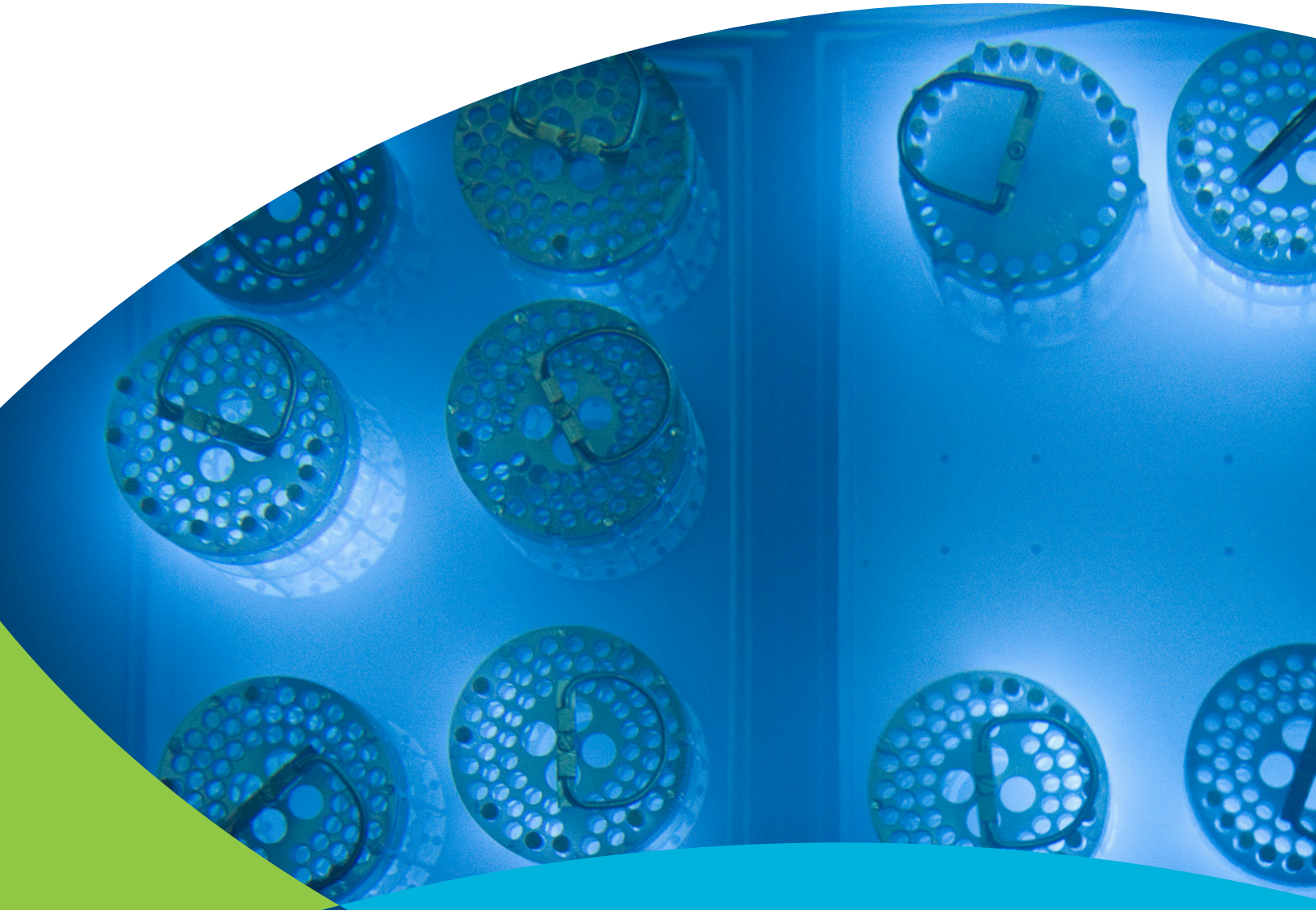
Gamma:
the heart of radiation sterilization past, present and future



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Executive Summary

The COVID-19 global pandemic of 2020 has brought into sharp focus the critical role that the medical device supply chain plays in terms of bringing safe, effective healthcare to the world's population. A key part of this supply chain is the sterilization of these devices, historically accomplished primarily through the use of ethylene oxide and gamma irradiation, using Cobalt-60.

Recent pressure on the supply of Cobalt-60 – due to a temporary and unexpected reduction in global production capacity, coupled with higher than historical levels of demand – have caused some to call into question the long-term viability of gamma sterilization, and pursue alternate modalities, some of which have yet to be proven at industrial scale. As switching modalities involves cost, regulatory and supply chain risk, it should only be done where warranted by a solid set of technical and commercial arguments.

This paper will provide a brief overview of the importance and contribution of gamma irradiation as a sterilization modality, with a focus on why it has grown to hold a significant position in the 50 years it has been in use. It will also provide clarity on the current and future state of Cobalt-60 supply, and demonstrate to stakeholders that there is no compelling reason to consider switching from a modality that continues to deliver efficacy, reliability and cost effectiveness.

Background

Production of Cobalt-60 in nuclear reactors dates back to the 1950s. Originally, it was used in teletherapy machines for the treatment of cancer, an application that still exists today. However, Cobalt-60's prevalence as a source of energy for the terminal sterilization of single-use medical devices started to grow in the 1960s and today it is one of the two primary modalities in use globally.

The appeal of gamma irradiation as a sterilization modality lies in its simplicity. While designs for gamma irradiation equipment and facilities continue to evolve to incorporate modern technology, such as controls systems for enhanced safety and efficiency, the basic mechanics of passing product around the radiation source to receive an appropriate sterilizing dose are straightforward. The equipment is reliable and easily operated and maintained.

Moreover, the science of sterilization using gamma radiation has been thoroughly studied and the effects on both the reduction of microorganisms and changes to material properties are well understood. Standards for sterilization are endorsed and accepted by regulatory bodies around the world, and providers of gamma sterilization and related services have a large body of knowledge from which to draw in order to validate this modality of sterilization for new products.

As a result of decades of evolution, the global infrastructure that supports gamma sterilization has achieved a level of both technical and market efficiency that is difficult to match.

Current State

A rough estimate of the proportion of sterilization modalities employed in North America is that 50% of single use devices are sterilized with ethylene oxide, 40% with gamma and 10% with other modalities, primarily electron beam. Historically, the growth of the Cobalt-60 market has been in the 2-3% range on a volume basis, driven largely by growth in the medical device sterilization segment, which accounts for 80% of Cobalt-60 use globally.

The network of nearly 300 gamma irradiation facilities that has been established during the long history of the industry provides robust capacity for supply chains that rely on the critical sterilization step to get life-saving products to patients and healthcare providers. Typical uptime for a gamma facility is in excess of 95%, but backup capacity exists in the instance where it is needed. In addition, more than 20 new irradiation facilities have been constructed in 10 countries since 2015, evidence that the business case for expansion of gamma capacity continues to be strong.

Gamma sterilization benefits from inherent scalability. That is, a facility can start with a small amount of Cobalt and grow capacity over time by adding more. Currently, there are approximately 400 million Curies (MCi) of Cobalt installed globally, but the licensed capacity is estimated to be in excess of 600 MCi, so there is significant room for growth, even without adding new facilities.

In terms of the supply chain for Cobalt-60 itself, there are currently five geographically diverse producers of Cobalt-60 sealed sources. Each of these producers has relationships with reactors for activation of Cobalt-59, hot-cell facilities for manufacture of finished product under approved quality systems, and containers for transportation of sealed sources to end users.

Cobalt-59 is mined.

Cobalt-59 adjuster rods are installed in a nuclear reactor and activated to become Cobalt-60, which takes ~18-60 months.

Nordion processes the Cobalt-60 into C-188 double encapsulated sources—the industry standard in performance, reliability, and service for industrial or medical use.

With an established distribution network, global regulatory expertise and logistics capabilities, Nordion ships Cobalt-60 C-188 sources to customers around the world.

Cobalt-60 shipments are routinely made to over 40 different countries. Class 7 (radioactive) material is transported by a team of specialist organizations including carriers, freight forwarders, regulators and port authorities, with a wealth of knowledge around how to safely and securely transport this material.

The Facts about Cobalt Supply

Much of the recent discussion around alternative modalities to gamma is the result of a perturbation in the Cobalt-60 supply that had its origins in the 2014 failure of the REVISS joint venture between a Russian state owned enterprise and a British company. This failed joint venture resulted in an almost immediate reduction in the volume of Cobalt-60 accessible to the global market. At roughly the same time, the Embalse reactor in Argentina was shut down for refurbishment, removing additional Cobalt-60 from the global supply volume.

It is a testament to the robustness of Nordion's supply chain that the unexpected reduction in production volume from Russia resulted in very little disruption to the market overall.

The general strategic approach employed by Nordion for long-term Cobalt supply is to bring on new sources in advance of market needs and carry inventory, in order to buffer against such situations and provide flexibility for users. Nordion's inventory was able to sustain the entire market in 2014, as well as increased demand for the next several years as the Russian supply chain gradually came back online.

And while Russian supply has increased from 2014 levels, the supply chain has not yet returned to its pre-2014 state. The Embalse reactor has also been successfully refurbished and returned to service, and will realize its first post-refurbishment harvest of Cobalt in 2021. Exacerbating this protracted period of reduced global supply, the demand for Cobalt grew at more than twice the normal rate through 2018 and 2019.

Nordion's response to this confluence of events has been the implementation of a temporary allocation program, in order to ensure that in an environment of tight supply, there is fair and equitable distribution of Cobalt. It is also important to note that Nordion shipped more Cobalt in 2019 than 2018, and expects to increase that amount again in 2020. At the same time, the global supply chain continues to evolve to respond to the dynamics of demand, as detailed in the next section.

Nordion estimates that, globally, demand exceeds supply by approximately 5%. This shortfall is being felt more in China, South America and South East Asia, regions that depend less on Nordion supply and more on the other suppliers, who have experienced disruptions. Nordion is fulfilling all of its contractual supply commitments, and no customer is being sold less than they have contractually committed to purchase. Almost all North American and European users are receiving 100% of the Cobalt they request; these users are receiving more Cobalt in 2019 and 2020 than they received in 2017 and 2018.

Future State

As has always been the case, sources of Cobalt supply ebb and flow over time. New reactors are brought on line as justified by market demand. Supply is turned off when not needed, or when reactors reach the end of life. The industry is equipped to deal with these dynamics, as it has over the course of the last half century. Of course, responding to change takes time and an ongoing investment, both in terms of dollars and resources. Currently, Nordion has plans for significant investments in new supply.

Nordion has been consistent in the application of a Cobalt-60 supply strategy we call **Extend**, **Expand** and **Develop**, with the recent addition of **Unlock**. Following is a description of each of these strategic elements, along with specific initiatives and current status.

Extend: This strategy involves extending supply contracts with our existing suppliers, with whom we have had very successful relationships, some lasting more than 4 decades.

Initiative	Description	Status
Bruce Power	Largest supplier of Cobalt-60 globally, produces Cobalt in 4 CANDU units	Agreement extended to 2064. Reactors currently entering refurbishment
Pickering	Longest standing supplier of Cobalt-60, currently producing in 3 CANDU units	Agreement extended to end of life for reactors, forecasted to be 2024, with a possible extension to 2025

Beyond Nordion initiatives, refurbishment of reactors such as Embalse in Argentina, mean that Cobalt production can continue for 25-30 years.

Expand: The objective of this strategy is to use the existing CANDU and RBMK technology to convert reactors that are not currently producing Cobalt. This creates a broader range of opportunities, and could further diversify the supply mix geographically since many of these reactors operate outside of Canada.

Initiative	Description	Status
Cernavoda	2 CANDU-6 units operated by SNN in Romania	Technical feasibility study under way
RBMKs	Rosenergoatom operates 9 RBMK reactors in Russia	Production at LNPP reactors expanded to 4 additional reactors at Kursk and Smolensk
Darlington	Ontario Power Generation operates 4 CANDU units at Darlington	Units in refurbishment. Cobalt conversion program in detailed design phase

Develop: This strategy aims to develop new reactor technology for production of Cobalt in other reactor designs, such as Light Water Reactors (LWRs), that are more prevalent than CANDU and RBMK reactors, improving scalability (80% of the ~440 operating reactors globally are LWRs).

Initiative	Description	Status
Westinghouse	Develop technology for production of Cobalt-60 in Pressurized Water Reactors	Preliminary design of Cobalt targets and harvesting technology. Engagement of utility partners

Unlock: This approach leverages production capacity outside of Nordion's supply chain to bring Cobalt to the global market that might otherwise be inaccessible due to lack of transportation and logistics infrastructure.

Initiative	Description	Status
BRIT	The Board of Radioisotope Technology in India produces Cobalt in Pressurized Heavy Water Reactors	In 2019 and 2020, Nordion and BRIT collaborated to bring Indian Cobalt to the global market
TongXing	TongXing produces Cobalt in 2 CANDU-6 reactors in China	Since 2018 Nordion and TongXing have collaborated to bring Chinese Cobalt to the global market

In addition to increasing long-term supply, there are measures being taken by operators of gamma facilities to improve efficiency, thereby reducing overall demand. These include upgrades to equipment, better scheduling, and the use of mathematical modelling to reduce downtime for Cobalt-60 loading and product qualification.

Summary & Conclusion

Gamma sterilization using Cobalt-60 has a long history of efficacy built around a robust network of providers and facilities, well-developed science, technology and standards and diverse, flexible supply chains.

Alternate technologies for radiation sterilization, particularly x-ray, are being developed, but are still in relative infancy with respect to broad industry adoption. While much work has been done to advance the technology and the understanding of it, much work remains.

As such, the decision to switch modalities for existing products, or place new products in a modality without an established track record should be done with care, and a clear understanding of both the benefit and cost of doing so.

Despite recent challenges in the broader supply chain for Cobalt-60, Nordion's supply chain has continued to operate as expected, and was key in mitigating the global impact of a shortage. Nordion's leadership in the Cobalt-60 market, along with significant ongoing investments as part of the Extend, Expand, Develop and Unlock strategy, puts the global industry in a strong position for long-term growth.

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