A Billion Curies and Counting
50 years of Canadian nuclear innovation in healthcare

Canadian Nuclear Society, Ottawa Chapter
1 February 2016
Agenda

• A brief history
• Innovation drivers
• Some examples
  – New Mo-99
  – GCE R&D
  – HSA at Bruce B
  – Recycling
• What’s next?
A Brief History

1946: Eldorado Mining Inc.
1952: Comm Prod Div (AECL)
1964: First irradiator, C-188
1971: Move to Kanata
1978: Radio Chemical Company, TRIUMF
1987: Canadian Irradiation Centre
1988: Nordion International
1991: MDS
2010: Nordion (Canada) Inc.
2014: Sterigenics International
Nordion is a health science company that provides market-leading products used for the prevention, diagnosis and treatment of disease.

We’ve been delivering safe, high-quality products to global customers for more than 60 years.

To best serve the diversity of our customers’ requirements, we are organized into two business units—Gamma Technologies and Medical Isotopes.
Nordion’s Global Footprint

Approximately 375 employees
Around 30 products
Supply over 500 customers
Across more than 40 countries
Gamma Irradiation Applications

- Gamma is used for the irradiation of:
  - Medical Devices
  - Spices
  - Laboratory Products
  - Pharmaceuticals
  - Human Tissue Products
  - Pet Products
  - Natural Supplements
  - Cosmetics
  - Food
Cobalt-60 Production

- **Mine**: Plant manufactures Cobalt-59 pellets and slugs.
- **Manufacturer**: Plant assembles the source elements and adjusters, and then delivers them to the reactors.
- **Nuclear Reactors**: The Cobalt-59 adjuster rods are installed in the reactor and the Cobalt-59 is activated to become Cobalt-60. This process takes approximately 18-24 months.
- **Shipping Vehicle**: The Cobalt-60 is removed from the reactor and shipped to the processing facility.
- **Isotope Processors**: At the processing facility, the Cobalt-60 is processed into sources for industrial or medical use.
- **Shipping Vehicle**: The sources are shipped to the customer.
Cobalt-60 Production
Cobalt-60 source: C-188
JS-10000 Hanging Tote Irradiator
**Medical Isotopes**

- Medical isotopes are used to prevent, diagnose and treat disease.
- Main isotope supply sources are nuclear reactors and cyclotrons.
- Primary product is Mo-99, which decays for use in Technetium-99 (Tc-99m) generators, used in imaging to diagnose heart disease and cancers.
- Other Key Reactor Isotopes:
  - Xenon-133 (Xe-133), used in lung scans;
  - Iodine-131 (I-131), used to treat hyperthyroidism, thyroid cancer and non-Hodgkin’s lymphoma;
  - Iodine-125 (I-125), used to treat prostate cancer;
  - Yttrium-90 (Y-90), used to treat liver cancer.
- Key Cyclotron Isotopes:
  - Iodine-123 (I-123), used to diagnose thyroid disease;
  - Strontium-82 (Sr-82), used to manufacture rubidium-82 generators, which are used in imaging to diagnose heart disease;
  - Thallium-201 (Tl-201), used to diagnose and assess risk of coronary artery heart disease;
  - Palladium-103 (Pd-103), used to treat prostate cancer;
  - Indium-111 (In-111) and Gallium-67 (Ga-67) (both used to diagnose infection and cancer) at our Vancouver facilities.
Mo-99 Supply Chain

NUCLEAR REACTORS
- Irradiation of HEU targets to produce crude isotopes

MEDICAL ISOTOPE PROCESSORS
- Purification of Mo-99 and distribution to global radiopharmaceutical manufacturers

RADIOPHARMACEUTICAL MANUFACTURERS
- Tc-99m Generator manufacturing and distribution to radiopharmacies

RADIOPHARMACIES AND HOSPITALS
- Unit dose compounding and distribution to hospital/departments

PHYSICIANS AND PATIENTS
- Critical physiological diagnosis enabling informed therapeutic decisions

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Innovation Drivers

- Business growth
- Customer requirements
- Competition
- Regulatory environment
- Supply chain
Capacity for Innovation

- Radiation protection & health physics
- Electro-mechanical engineering
- Regulatory affairs
- Radiation physics
- Radiochemistry
- Nuclear security
- Package engineering
- Transportation and logistics
- International affairs
• Nordion’s current supply chain utilizes the National Research Universal (NRU) reactor operated by Canadian Nuclear Laboratories (CNL)

• The NRU is scheduled to cease routine production of Mo-99 in November 2016.

• Government of Canada announced on February 6, 2015 its support of the extension of the NRU operations until March 31, 2018 to help support global medical isotope demand in the unexpected circumstances of shortages during this time.

• Nordion supports the efforts of the Canadian Government to operate the NRU and provide a standby Mo-99 capability during the period of transition as new supply capacity comes online.
Nordion Future Mo-99 Supply Options

Since 2008 Over 50 worldwide files/projects have been evaluated
- Both Reactor and Accelerator-Based

Supply Selection Criteria
1. Non HEU-based technology/targets
2. Credible Partners
3. Leverages existing infrastructure/capabilities to drive efficiency
4. Commercial feasibility – for Nordion and partners
5. Timeline - potential for commercialization in the near term
Highly Credible Partners

General Atomics

**Target and reactor systems design and manufacturing**
- Trusted resource of high-technology systems
- Experts in nuclear fuel cycle, including uranium mining and processing
- Experts in reactor design: GA TRIGA® research reactors in operations around the world for over 50 years
- Developer of LEU technology utilizing novel reusable target design

Missouri University Research Reactor (MURR)

**Premium Reactor Operator and Research Center**
- 10 megawatt facility; the largest university research reactor
- Operates 52 weeks a year
- 35+ years of successful and innovative radiopharmaceutical R&D and collaborations with industry
- Strong record of regulatory compliance (US NRC, US FDA)
- Experts in volume radiochemical processing and international shipping
- Nordion’s partner in supply of TheraSphere for over 20 years

Nordion

**Premier Isotope Producer and Distributor**
- Experts in Mo-99 purification into medical grade product since 1975
- Strong record of regulatory compliance (US FDA, EMEA, Health Canada)
- cGMP/GLP - licensed facility
- Global leading supplier of Mo-99 with extensive marketing, sales & distribution expertise
- Global licensed transport container fleet
Selective Gas Extraction (SGE)

**Step 1**
LEU target irradiated; forms new radioisotopes

**Step 2**
Gas introduced to target in-situ; desired isotopes are converted to volatile compounds

**Step 3**
Gas extracted with desired isotopes and transported to collection system
Changes in the Healthcare Landscape

- New materials
  - New capabilities
  - New sterilization challenges
- Combination products
- Biomaterials
- Human tissue
- Next generation devices
Challenges with sensitive products

• Material compatibility
• Temperature management
• Tight dose ranges
• Turnaround time
• Inventory
Compatibility

- Interaction of radiation with polymers
Sterilization Science at Nordion

• Gamma Centre of Excellence (GCE)
  – Outreach to new and existing users of gamma to help solve specific challenges through collaborations
  – Targeted research to seek collaboration partners and enhance our own knowledge in gamma applications and effects
Case Studies

- Low temperature irradiation
- Human tissue and biologics
- Biomaterials for Drug Delivery
- Bioresorbable Medical Devices
- PTFE irradiation
- Next Generation Devices
Low Temperature Irradiation
Tensile Strength

**Polypropylene**

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**Latex**

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Biological Indicator Data – Fraction Negative

- Fraction negative uses 8kGy and up
- D10 increases with decreasing temperature

*B. pumilus* D10 Values - Low Temperature Study
## Results of Biomaterials

- **PEG and PLGA**
  - Dynamic light scattering DLS
  - PEG – Frozen conditions showed lowest degradation
  - PLGA – RT and 0°C conditions showed lowest degradation
  - Drug delivery in cancer and spinal cord injuries

<table>
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<th>Temp (°C)</th>
<th>% of Original Material</th>
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• Electron beam study revealed protective effect
  – Huy Nguyen
  Masters Thesis, August 2014

• Next steps, gamma study with colder temperatures and combined cold/inert
CBRAM® Gamma Tolerance Study

Unexposed  50 kGy  100 kGy  200 kGy

Demonstrated immunity to gamma sterilization at 8x the typical dose (200 kGy)

Test Results so far on Adesto CBRAM

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<td>100 kGy</td>
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<td>200 kGy</td>
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Adesto-Nordion 2013 Study

Adesto-Nordion 2014 Study
High Specific Activity (HSA) Co-60

- Typically produced in research reactors today
  - NRU (Chalk River)
  - ATR (Idaho Falls)
  - Russia

- Typical Specific Activity required: 280 Ci/gm – 320 Ci/gm

- The two largest markets for HSA:
  - External beam Radiotherapy
  - Stereotactic Radiosurgery

Smaller quantities are also used for:
- Special sources:
  - Calibration standards, Rad-hardness testing, Research applications
- Non-Destructive Testing
External Beam Radiotherapy

- Over 60 years of clinical experience
- Efficient and effective cancer therapy
- Delivering thousands of cancer treatments daily
- Large installed base in developing world
- Next generations of treatment have developed successfully…
Stereotactic Radio-Surgery

- Non-invasive method for treating brain disorders
- Single, high dose of irradiation to a small and critically located intra-cranial volume through the intact skull.
MRI Guided Radiation Therapy

- Combines the effectiveness and efficiency of gamma-based radiotherapy with the accuracy of MRI to minimize damage to healthy tissue.

- Three treatment heads are used and the beam is adjusted during treatment based on an MRI developed target area.
LSA (Slug) vs HSA(Pellet)

6.5g vs 0.007g

Different final forms
Primary HSA Supply Picture

- NRU & ATR
  - Up to 2013

- NRU
  - 2013-2018

- NRU & ATR
  - 2018-2019

- BP & ATR
  - 2019 onward
C-188 Cobalt-60 source lifecycle

Return of spent sources

Sources shipped to customers

20+ years in service

Nordion Source Production Facility

Fresh cobalt

Spent cobalt

Reactors
Optimized for Recycling

Fresh Cobalt slugs

Spacers
What’s Next?

• Mo-99
• Extend/Expand/Develop
• New disposal paths
• Safety and security
• Food irradiation