Harvesting of legacy radium sources; experiences and approaches at BWXT Medical

Dr. Patrick Causey,
Richard Decaire, RSO,
May 30, 2024

Timeline of BWXT's presence in nuclear medicine

1950-1960's
Canadian Nuclear Labs allows distribution of isotopes for commercial purposes

1970-1980's
Canadian Nuclear Labs establish research facilities and begin producing Mo-99

1990's
TRIUMF and Nordion enter into long term irradiation agreement

1991
Nordion (a conglomeration of Canadian facilities and capabilities) acquired by MDS Health Group

2014
Nordion purchased by Sotera Health for $805 million

1950 1960 1970 1980 1990 2000 2010

Nordion

Producing Mo-99 with sporadic industry disruptions

BWXT

Producing and handling nuclear isotopes

1950 1960 1970 1980 1990 2000 2010

1950's
Begins making nuclear systems for US Navy

1999
Begins producing uranium targets for Mo-99 production

2016
BWXT begins Neutron Capture R&D

2018
BWXT acquires Nordion medical isotopes business

2022
BWXT Medical files for FDA approval of Tc-99 generator

BWXT Medical

2019-2022
BWXT Medical stands up Tc-99m production effort and builds product portfolio

2021
Regulatory approval to install Darlington irradiation system

Global Leader in **Nuclear Medicine Manufacturing**

BWXT has capability, partners and full product offering

Full Product Offering

	Active Pharmaceutical Ingredients				Sterile Drugs	CDMO[1]
	PET	SPECT	Therapeutics			
In-Market	^{82}Sr, ^{68}Ge	^{111}In, ^{123}I	^{225}Ac	API Sterile Drugs	^{111}In Oxine, ^{123}I MIBG	^{90}Y TheraSphere™
Pending	^{64}Cu, ^{89}Zr	^{203}Pb	^{177}Lu, ^{67}Cu, ^{212}Pb	Contract Drug Manufacturing (CDMO)	^{99}Tc	^{225}Ac, ^{177}Lu, ^{111}In

^{225}Ac

Actinium-225 Chloride - Spallation
Active Pharmaceutical Ingredient

- Actinium-225 Chloride is an active pharmaceutical ingredient for Ac-based radiopharmaceuticals.
- The radioisotope is manufactured following high-energy proton spallation of natural thorium metal to produce the parent isotope, radium-225, as the integral component in a radium generator.
- Ra-225 beta decays with a 15 day half-life, producing high quality final product.
- No detectable Ac-227, observed in other spallation processes for direct production of actinium-225.
- Planned Drug Master Filing

BWXT Medical

Type 1B Licence implications

Items that need addressing for Ra-226:

- Derived Release Limits for environmental protection –if you don't have published values
- Update to Preliminary Decommissioning Plan (and Financial Guarantee)

Other:

- Our licence permits us to "possess, transfer, use, process, import, manage, store or dispose of nuclear substances" including Ra-226
- *CNSC reporting requirements specific to Ra-226 sources greater than 10 Ci (0.4 TBq):*
  - 7 days before any transfer or export
  - 48 hours after receipt

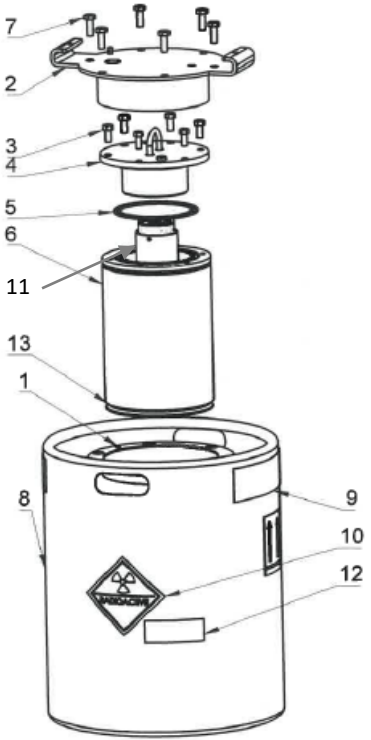
Licence elements in this presentation

- Management,
- Training,
- **Operations**,
- Reporting,
- Safety Analysis,
- Design,
- Fitness,
- **Radiation Protection**,
- Health and Safety,
- **Environmental Protection**,
- **Waste Management**,
- **Packaging/Transport** and
- Security

Packaging and Transportation Solutions

Parts List

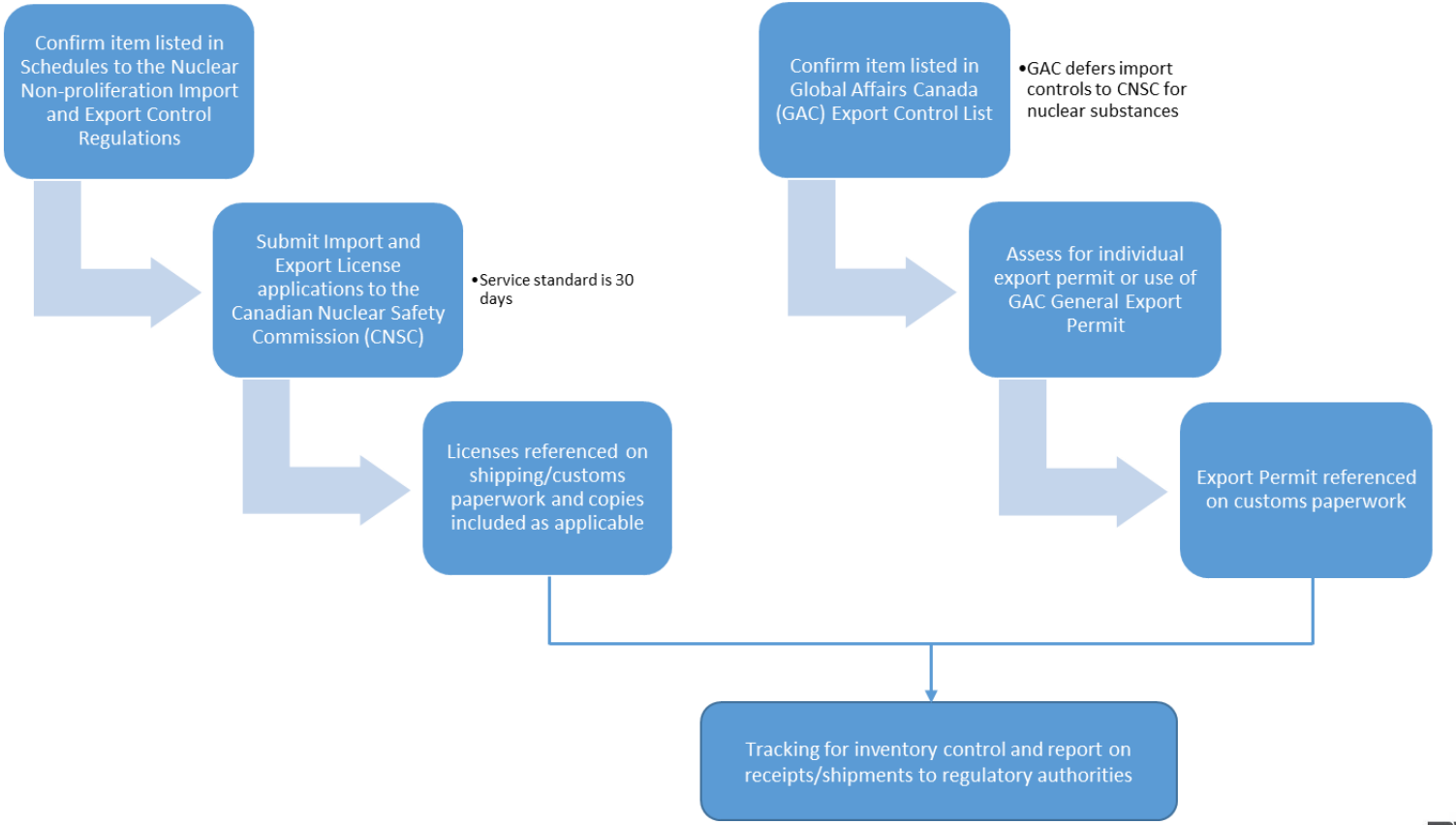
1. Wire seal
2. Lid
3. Hex screws
4. Shielded plug
5. O-ring
6. Lead shielding
7. Steel bolt
8. SS cylinder
9. Shipping container ID
10. Category label
11. Leak-proof insert
12. UN Number label
13. Gasket



- F-707 for Type ‘A’ quantities of radioisotopes (81 mg, 3 GBq Ra-226).
  - **Approved**
- F-458 for Type ‘B’ quantities of radioisotopes.
  - *Currently in process of obtaining licence approvals*

- Packages have the following components:
  - A receptacle (vial or bottle) containing the isotope.
  - A leakproof insert (*e.g.* F-248),
  - A shielding vessel,
  - Outer packaging, and
  - Tamper-proof seal

Canadian Regulatory Requirements for Import/Export of Radium-226



Hot Cell Facilities

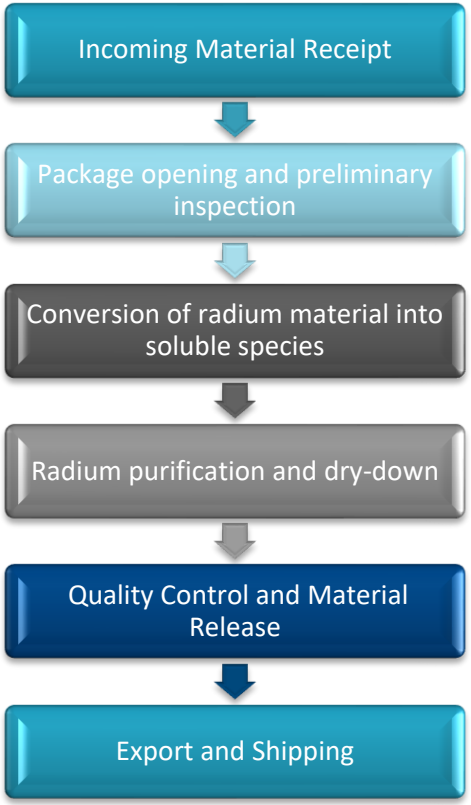
- BWXT's Kanata site is a Processing Facility which formerly manufactured **radioiodines** and **radioxenons** (Helpful experience for radon trapping and breathing air monitoring)
- Nuclear ventilation and process equipment used to locally control radon-222
- Cells are currently undergoing upgrading and commissioning activities
- All work is controlled through existing Safety and Radiation Protection Programs

BWXT Medical Products/Sevices in Development

^{226}Ra

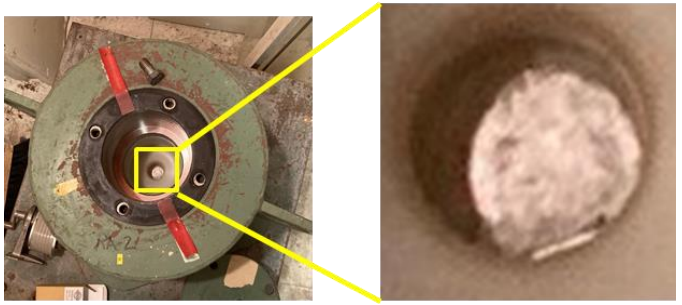
Radium-226 salt
Radiochemical Precursor

- BWXT has developed a Process identifying key steps and decision points for the recovery of Ra-226 from legacy sources
- Acknowledges the diversity of source materials and is initially targeting brachytherapy sources
- Recognizing the significant lack of information that often accompanies these types of legacy radioactive sources
- Currently in Development space, all documentation are ‘R-docs’
- **Successfully and safely executed Proof of Concept radium harvesting from Category 2 sealed source in Kanata**



Proof of Concept Harvesting

- BWXT had in our inventory mg-sized Ra-226 sealed source
- All work was controlled under our Work Permit program
- Work was executed in our radiological R&D lab
- Radiation field ~ 4 R/h near contact
- Successfully controlled Rn-222
- Analytical method are in the development phase
  - γ-spectroscopy
  - ICP-MS
  - α-spectroscopy
  - all methods will be qualified



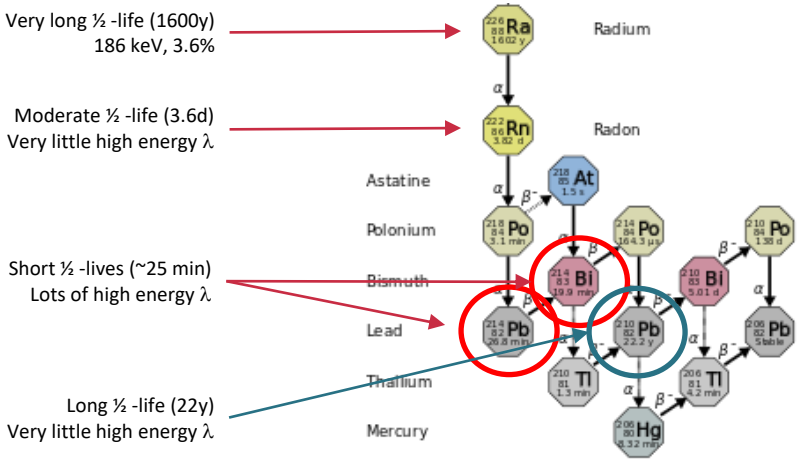
Trapping of Rn-222 during sealed source processing

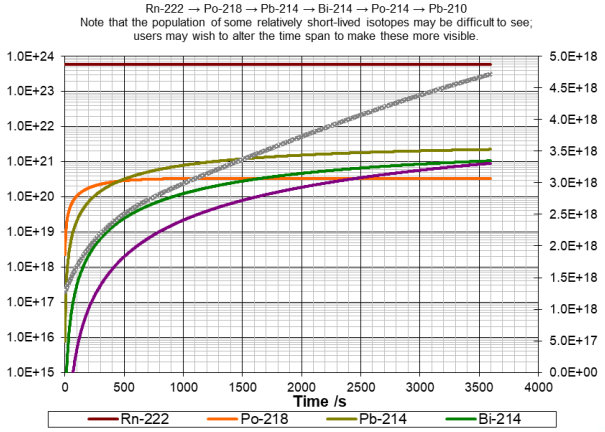
By interrupting the decay chain, legacy radioxenon traps were **extremely effective** in capturing radon!

Grow-in dose rates from Rn-222 extracted process gases were as modeled in MicroShield.

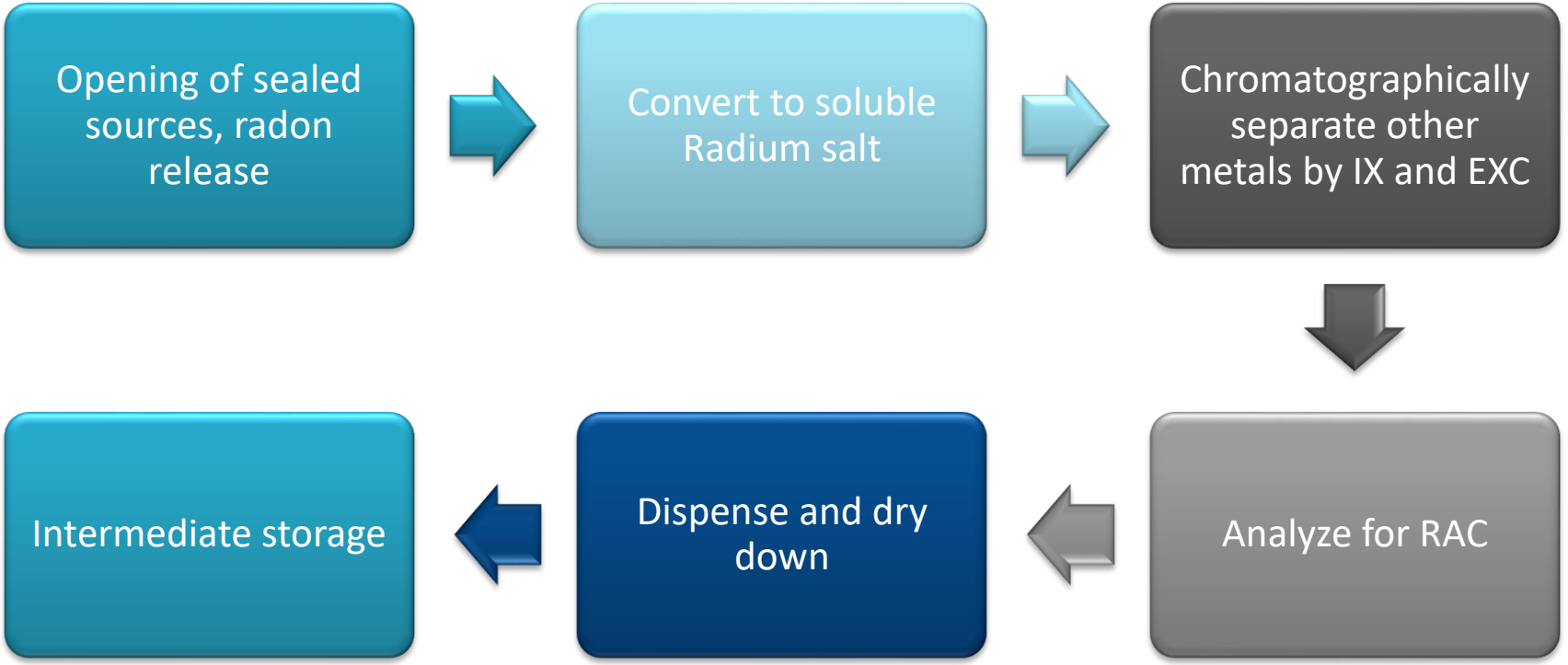
Shouldn't have been surprising, but it still felt that way…

Elapsed Time	Radiation Field Measurement (mR/h)
0	0.7
1	1392
2	2235
3	2467



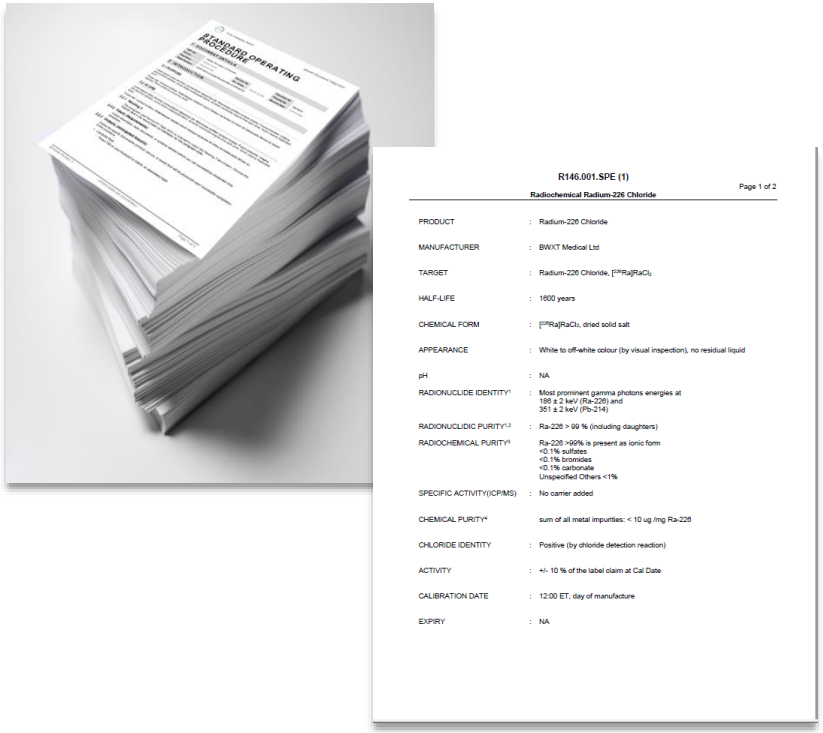


Simplistic Chemical Processing

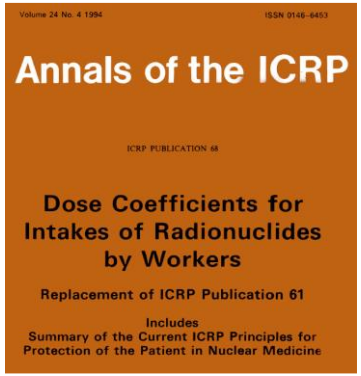


Generated following Proof of Concept work on sealed Radium Source

- Developed Process Flow for receipt and handling of legacy radium sources
- Drafted SOPs for opening and isolation of Special Form Capsules and sealed radium sources from customers/partners
- Drafted SOPs for chemical processing of opened sources, a combination of EXC and IX
- Qualified analytical methods for ICP-MS, and γ-spectroscopy for ^{225}Ac
- Preliminary material specifications



Implications of ICRP 68 vs. ICRP 137



ICRP Publication 137

Occupational Intakes of Radionuclides: Part 3

66 THE REPORT OF A TASK GROUP OF COMMITTEE 2

Table B.1.—(*continued*)

Nuclide	$t_{1/2}$	Effective dose coefficients (Sv Bq^{-1})					
		Inhalation, $e_{inh}(50)$				Ingestion	
		Type	f_1	1 μm AMAD	5 μm AMAD	f_1	$e_{ing}(50)$
Radium							
Ra-223	11.4d	M	0.200	6.9E-06	5.7E-06	0.200	1.0E-07
Ra-224	3.66d	M	0.200	2.9E-06	2.4E-06	0.200	6.5E-08
Ra-225	14.8d	M	0.200	5.8E-06	4.8E-06	0.200	9.5E-08
Ra-226	1.60E+03y	M	0.200	1.6E-05	1.2E-05	0.200	2.8E-07
Ra-227	0.703h	M	0.200	2.8E-10	2.1E-10	0.200	8.4E-11
Ra-228	5.75y	M	0.200	2.6E-06	1.7E-06	0.200	6.7E-07

13.4. Dosimetric data for radium

Table 13.7. Committed effective dose coefficients (Sv Bq^{-1}) for the inhalation or ingestion of ^{226}Ra and ^{228}Ra compounds.

Inhaled particulate materials (5-μm AMAD aerosols)	Effective dose coefficients (Sv Bq^{-1})	
	^{226}Ra	^{228}Ra
Type F, nitrate	1.6E-07	4.1E-07
Type M, all unspecified forms	1.4E-06	1.2E-06
Type S	1.3E-05	2.2E-05
Ingested materials		
All forms	1.3E-07	3.4E-07

AMAD, activity median aerodynamic diameter.

BWXT Medical

New ICRP series has a software viewer with IRF's, individualized chapters on elements and data on multiple isotopes

Electronic Annex / OIR Data Viewer

Dose per Intake | Dose per Content & Reference Bioassay Functions | Radon

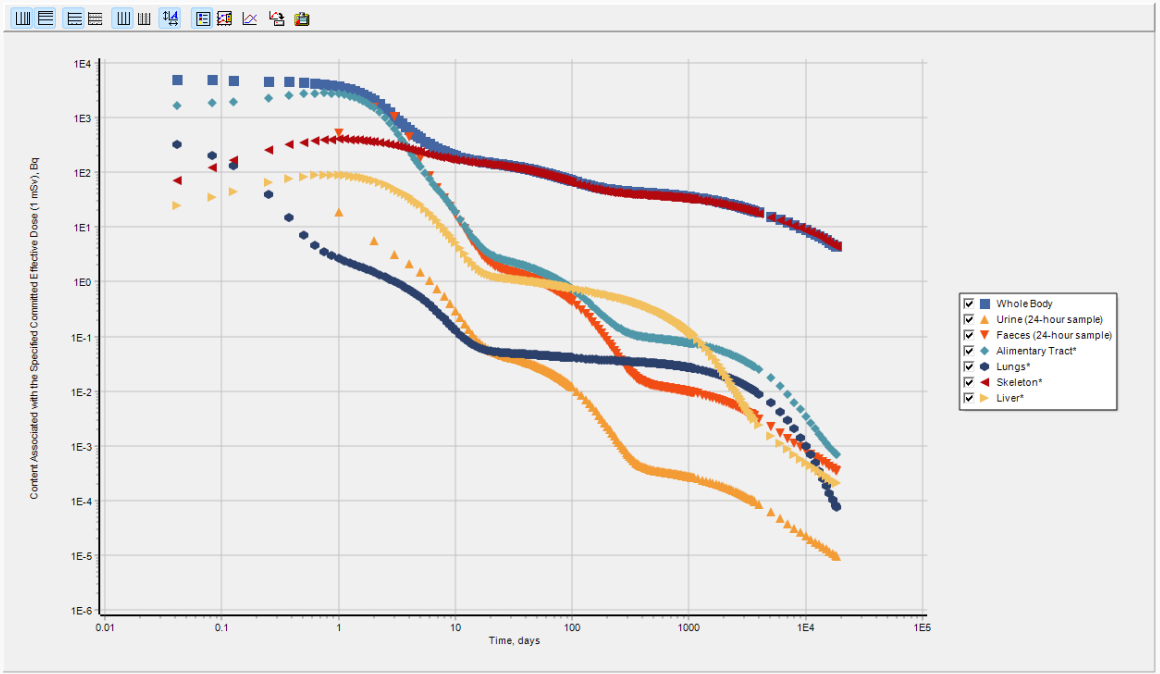
Intake Parameters

Radionuclide: Ra 226

Route of Intake: Inhalation

Material: Aerosols Type F, Nitrate, f_A=0.2

AMTD/AMAD, µm: 5



Displayed Data

- Dose per Content Function
- Content for the Specified Dose 1 mSv
- Content per Intake (Reference Bioassay Function)

Content in an Organ or Excreta Sample Associated with the Specified above Committed Effective Dose (1 mSv), Bq

Time, days	Whole Body	Urine (24-hour sample)	Faeces (24-hour sample)	Alimentary Tract*	Lungs*	Skeleton*	Liver*
0.041667	5.0E+3	-	-	1.6E+3	3.2E+2	7.2E+1	2.4E+1
0.083333	4.9E+3	-	-	1.8E+3	2.0E+2	1.2E+2	3.5E+1
0.125	4.8E+3	-	-	2.0E+3	1.3E+2	1.7E+2	4.5E+1
0.25	4.7E+3	-	-	2.3E+3	4.0E+1	2.6E+2	6.5E+1
0.375	4.5E+3	-	-	2.5E+3	1.5E+1	3.2E+2	7.7E+1
0.5	4.4E+3	-	-	2.7E+3	7.2E+0	3.5E+2	8.4E+1
0.625	4.3E+3	-	-	2.8E+3	4.6E+0	3.8E+2	8.8E+1
0.75	4.1E+3	-	-	2.8E+3	3.6E+0	3.9E+2	9.0E+1
0.875	3.9E+3	-	-	2.8E+3	3.0E+0	4.0E+2	9.0E+1
1	3.7E+3	1.9E+1	5.2E+2	2.7E+3	2.7E+0	4.0E+2	9.0E+1
1.125	3.5E+3	-	-	2.6E+3	2.4E+0	4.0E+2	8.8E+1
1.25	3.3E+3	-	-	2.5E+3	2.2E+0	4.0E+2	8.6E+1
1.375	3.1E+3	-	-	2.4E+3	2.1E+0	4.0E+2	8.4E+1
1.5	2.9E+3	-	-	2.2E+3	1.9E+0	3.9E+2	8.2E+1
1.625	2.7E+3	-	-	2.0E+3	1.8E+0	3.8E+2	7.9E+1
1.75	2.5E+3	-	-	1.9E+3	1.7E+0	3.8E+2	7.6E+1
1.875	2.3E+3	-	-	1.7E+3	1.6E+0	3.7E+2	7.4E+1
2	2.1E+3	5.7E+0	1.5E+3	1.5E+3	1.5E+0	3.6E+2	7.1E+1
2.25	1.8E+3	-	-	1.2E+3	1.4E+0	3.5E+2	6.5E+1
2.5	1.5E+3	-	-	1.0E+3	1.2E+0	3.3E+2	6.0E+1
2.75	1.3E+3	-	-	8.0E+2	1.1E+0	3.2E+2	5.5E+1
3	1.1E+3	3.2E+0	1.0E+3	6.3E+2	1.0E+0	3.1E+2	5.1E+1
3.25	9.0E+2	-	-	5.0E+2	9.4E-1	3.0E+2	4.7E+1
3.5	7.8E+2	-	-	4.0E+2	8.6E-1	2.9E+2	4.3E+1
3.75	6.8E+2	-	-	3.2E+2	7.9E-1	2.8E+2	3.9E+1
4	6.1E+2	2.1E+0	4.5E+2	2.6E+2	7.2E-1	2.7E+2	3.6E+1
4.25	5.4E+2	-	-	2.1E+2	6.7E-1	2.6E+2	3.3E+1
4.5	4.9E+2	-	-	1.8E+2	6.1E-1	2.5E+2	3.0E+1
4.75	4.5E+2	-	-	1.5E+2	5.6E-1	2.4E+2	2.8E+1
5	4.2E+2	1.5E+0	1.8E+2	1.3E+2	5.2E-1	2.4E+2	2.5E+1
5.5	3.7E+2	-	-	9.6E+1	4.4E-1	2.2E+2	2.2E+1
6	3.3E+2	1.1E+0	8.8E+1	7.6E+1	3.8E-1	2.1E+2	1.8E+1
6.5	3.0E+2	-	-	6.1E+1	3.3E-1	2.0E+2	1.5E+1
7	2.8E+2	7.6E-1	5.1E+1	5.1E+1	2.8E-1	2.0E+2	1.3E+1
7.5	2.6E+2	-	-	4.2E+1	2.4E-1	1.9E+2	1.1E+1

*See the Key Term help for the explanation

Table 13.8. Dose per activity content of ^{226}Ra in lungs and in daily excretion of urine and faeces (Sv Bq^{-1}); 5-μm activity median aerodynamic diameter aerosols inhaled by a reference worker at light work.

Time after intake (d)	Type F			Type M			Type S		
	Lungs	Urine	Faeces	Lungs	Urine	Faeces	Lungs	Urine	Faeces
1	3.7E-04	5.2E-05	1.9E-06	2.8E-05	2.7E-03	1.6E-05	2.1E-04	5.2E-01	1.6E-04
2	6.6E-04	1.7E-04	6.5E-07	2.9E-05	7.4E-03	5.3E-06	2.2E-04	1.4E+00	4.9E-05
3	9.8E-04	3.1E-04	9.6E-07	3.0E-05	1.4E-02	8.0E-06	2.3E-04	2.7E+00	7.5E-05
4	1.4E-03	4.7E-04	2.2E-06	3.1E-05	2.0E-02	2.0E-05	2.3E-04	3.9E+00	2.0E-04
5	1.9E-03	6.7E-04	5.4E-06	3.1E-05	2.8E-02	6.4E-05	2.3E-04	5.5E+00	6.6E-04
6	2.6E-03	9.4E-04	1.1E-05	3.2E-05	3.8E-02	1.9E-04	2.4E-04	7.6E+00	2.3E-03
7	3.6E-03	1.3E-03	2.0E-05	3.3E-05	5.0E-02	4.3E-04	2.4E-04	1.0E+01	6.6E-03
8	4.7E-03	1.8E-03	2.9E-05	3.3E-05	6.5E-02	7.1E-04	2.4E-04	1.4E+01	1.3E-02
9	6.1E-03	2.5E-03	4.2E-05	3.4E-05	8.1E-02	9.8E-04	2.5E-04	1.8E+01	1.8E-02
10	7.7E-03	3.4E-03	5.8E-05	3.4E-05	9.9E-02	1.2E-03	2.5E-04	2.2E+01	2.2E-02
15	1.5E-02	1.1E-02	2.3E-04	3.6E-05	1.8E-01	2.7E-03	2.5E-04	4.8E+01	4.7E-02
30	2.0E-02	2.5E-02	6.6E-04	4.0E-05	2.5E-01	5.0E-03	2.6E-04	7.0E+01	1.2E-01
45	2.1E-02	3.2E-02	8.7E-04	4.5E-05	2.8E-01	5.8E-03	2.7E-04	7.7E+01	1.3E-01
60	2.2E-02	4.2E-02	1.1E-03	4.9E-05	3.1E-01	6.5E-03	2.8E-04	8.3E+01	1.4E-01
90	2.4E-02	7.1E-02	1.9E-03	6.1E-05	3.9E-01	8.2E-03	3.0E-04	9.4E+01	1.5E-01
180	2.7E-02	3.2E-01	8.8E-03	1.1E-04	7.5E-01	1.6E-02	3.5E-04	1.2E+02	2.0E-01
365	2.9E-02	2.1E+00	5.9E-02	3.6E-04	2.5E+00	5.6E-02	4.7E-04	1.7E+02	3.5E-01

Bioassay Capabilities

ICRP Publication 137

Occupational Intakes of Radionuclides: Part 3

Table 13.4. In-vitro monitoring techniques for ^{226}Ra.

Isotope	Monitoring technique	Method of measurement	Expedited detection limit*	Achievable detection limit†
^{226}Ra	Urine bioassay	α spectrometry	0.2 Bq L^{-1}	
^{226}Ra	Urine bioassay	Emanation	5 mBq L^{-1}	0.3 mBq L^{-1}
^{226}Ra	Urine bioassay	Proportional counting	4 mBq L^{-1}	
^{226}Ra	Urine bioassay	Liquid scintillation counting	3 mBq L^{-1}	
^{226}Ra	Urine bioassay	ICP-MS	1.72×10^{-10} mg L^{-1} ‡,§	
^{226}Ra	Faeces bioassay	Proportional counter	16 mBq $24\,h^{-1}$ ¶	

ICP-MS, inductively coupled plasma mass spectrometry.
*Short preparation time (5–8 h), not used in routine.
†Several weeks preparation time (20–30 d).
‡2–3 d preparation time.
§1.72×10^{-10} mg $L^{-1} = 6.3$ mBq L^{-1}.
¶Results were given in mg of ash and converted to mg d^{-1} by considering 4 g ash per daily faecal excretion.

Table 13.5. In-vivo monitoring techniques for ^{226}Ra.

Isotope	Monitoring technique	Method of measurement	Typical detection limit	Achievable detection limit
^{226}Ra	Lung measurement	γ-ray spectrometry, in vivo	100 Bq	40 Bq

Experience at BWXT Medical

commercial offerings
10 mBq/L
Urinalysis detection limit

Government offering
60 Bq - 1hr lung count detection limit
20 Bq - 8hr lung count detection limit

BWXT Medical

ICRP 137 implication of Bioassay Detection Limits

Type F - 24hr Urine	
Day1	0.5 µSv (0.05 mrem)
Day90	0.71 mSv (71 mrem)

Type M - 24hr Urine	
Day1	27 µSv (2.7 mrem)
Day90	4 mSv (400 mrem)

Type S - 24hr Urine	
Day1	5.3 mSv (530 mrem)
Day90	909.1 mSv (90.91 rem)

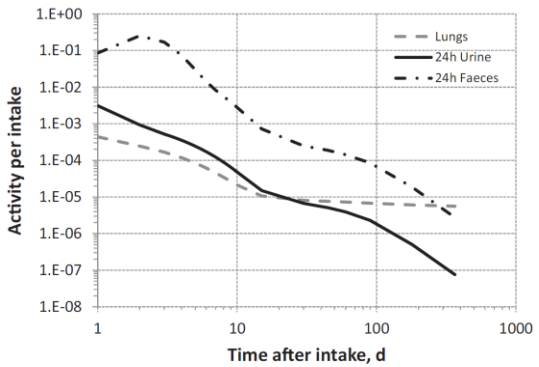


Fig. 13.2. Lung content and daily urinary and faecal excretion of ^{226}Ra following inhalation of 1 Bq Type F.

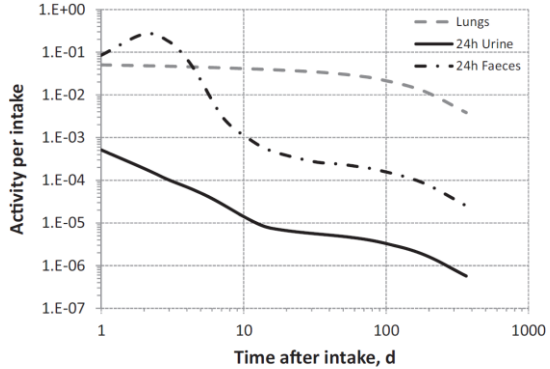


Fig. 13.3. Lung content and daily urinary and faecal excretion of ^{226}Ra following inhalation of 1 Bq Type M.

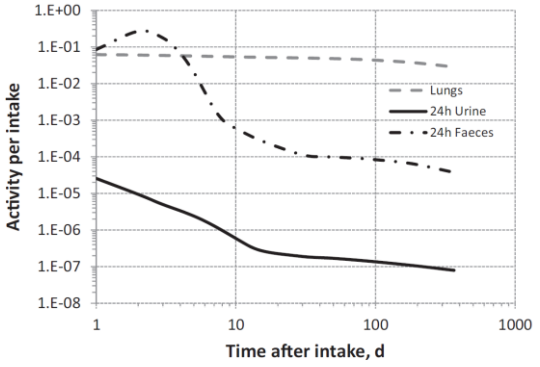


Fig. 13.4. Lung content and daily urinary and faecal excretion of ^{226}Ra following inhalation of 1 Bq Type S.

Type F -24hr Faeces @0.02 mBq DL	
Day1	0.04 µSv (0.004 mrem)
Day90	0.038 mSv (3.8 mrem)

Type M -24hr Faeces @0.02 mBq DL	
Day1	0.3 µSv (0.03 mrem)
Day90	0.167 mSv (16.71 mrem)

Type S -24hr Faeces @0.02 mBq DL	
Day1	3 µSv (0.3 mrem)
Day90	3.07 mSv (307 mrem)

Type F – Lung @ 50 Bq DL	
Day1	18.52 mSv (1.852 rem)
Day90	1190 mSv (119 rem)

Type M - Lung at 50 Bq DL	
Day1	1.39 mSv (139 mrem)
Day90	3.13 mSv (313 mrem)

Type S - Lung at 50 Bq DL	
Day1	10.64 mSv (1064 mrem)
Day90	14.71 mSv (1471 mrem)

BWXT Medical

Bioassay at BWXT Medical

Startup:

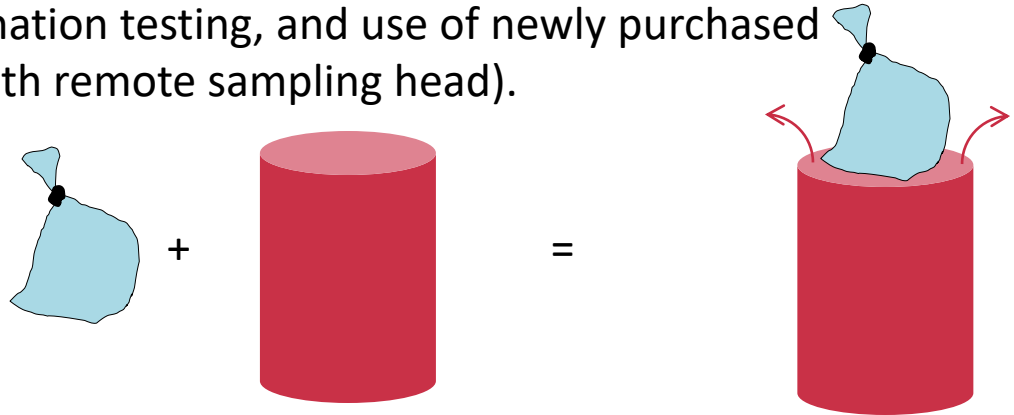
- Baseline urine and lung counting
- Then routine bioassay with campaign based frequency

  …Eventually expect to fall to a Special Bioassay Frequency

With more operating experience we expect to fall to a Special bioassay frequency … based on operating experience from contamination testing, and use of newly purchased iCAMs (one with remote sampling head).

Image provided courtesy of Mirion Technologies ©2024

- Incident



- Single taped bags Eventually off-gassed Rn, bag added months later = airborne Rn progeny

Conclusions

- BWXT has a long and documented history as a global leader in Nuclear Medicine Manufacturing
- Offering Active Pharmaceutical Ingredients, sterile Drug Products, bulk radiochemicals, and custom services
- Products and services, including Ac-225 and Ra-226, fall under a recognized Quality Assurance Program
- Wide range of critical capabilities in areas of Licensing, Regulatory, Transportation, Logistics and Quality
- Existing unique facilities and highly qualified personnel to support and execute complex projects

Contact Information

Process Questions:

Patrick Causey,
Technical Manager, Research and Development
BWXT Medical Ltd.
Mobile +1 343-548-2559
pcausey@bwxt.com

Radiation Safety Questions:

Richard DeCaire,
Senior Manager, Radiation Safety BWXT Medical
BWXT Medical Ltd.
Mobile +1 613-867-0578
rdecaire@bwxt.com

Strategic Supply and Business Development

Mike Flagg,
Director, Strategic Supply BWXT Medical
BWXT Medical Ltd.
Mobile +1 434-363-8484
mflagg@bwxt.com