Canadian Nuclear Safety Commission | Commission canadienne de sûreté nucléaire

Canada

Technetium 99m - from Reactors to Accelerators – Regulatory and Safety Aspects

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CNSC CCSN

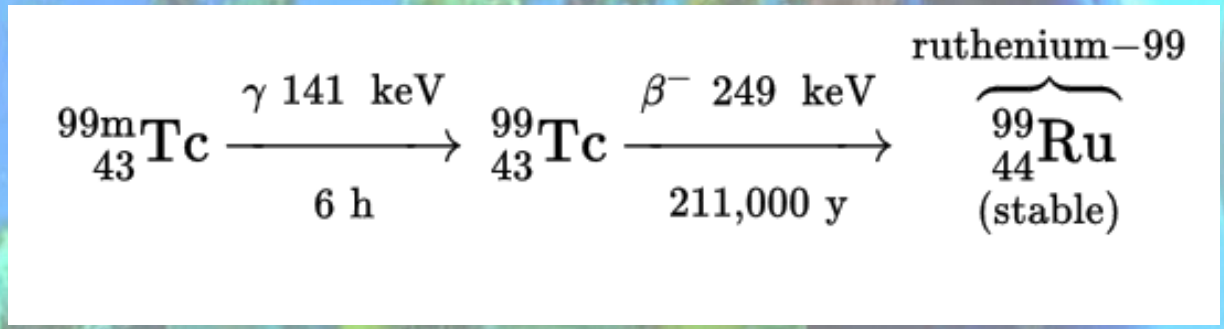
CANADA 150

Outline

- Introduction
- Canada as a global supplier
- Problem and opportunity
- CNSC's Regulatory Oversight
- Infrastructure development
- Almost there
- Conclusion

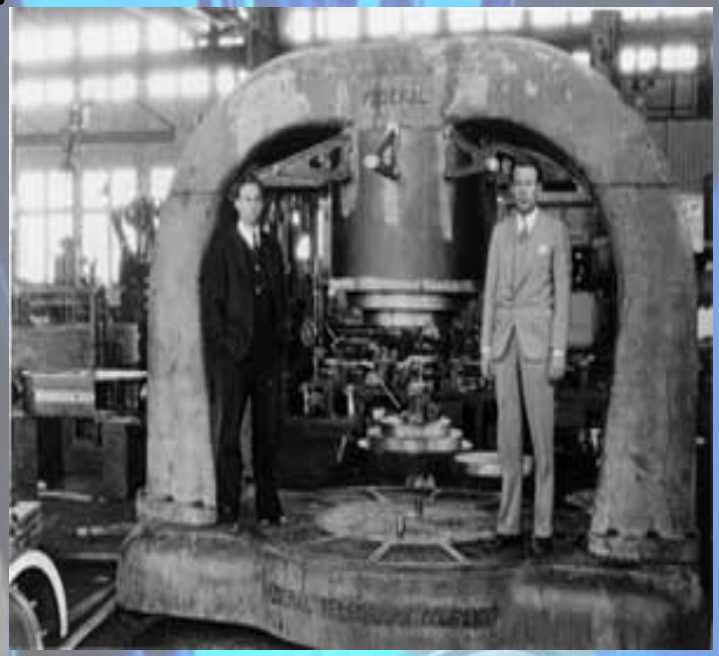
Technetium-99m

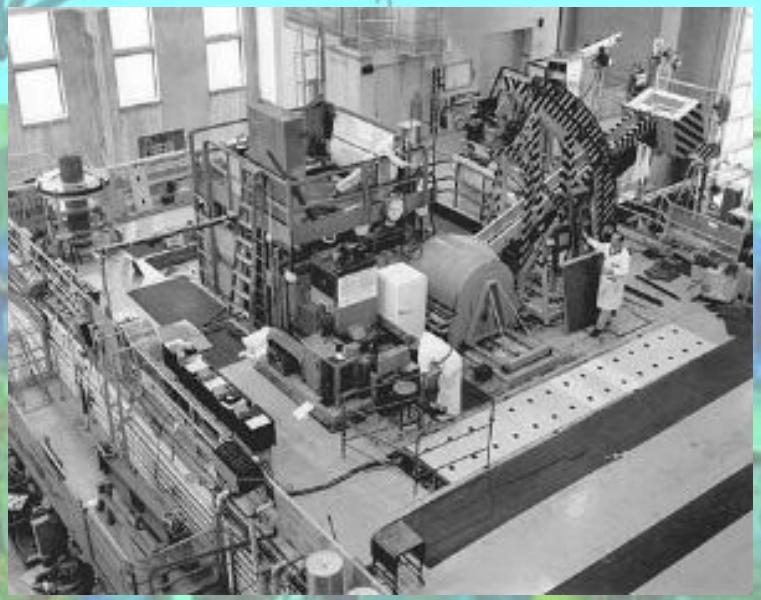
- Most commonly used medical radioisotope
- Preferred radiotracer for nuclear medicine imaging
  - high quality image
  - suitable gamma energy
  - low dose to patients
  - “available”
- 35 million examination per year worldwide
- 1.5 million procedures in Canada in 2015



Discovery

1st time, in Italy in 1937 in a sample of molybdenum irradiated by E.O. Lawrence, the inventor of the cyclotron.

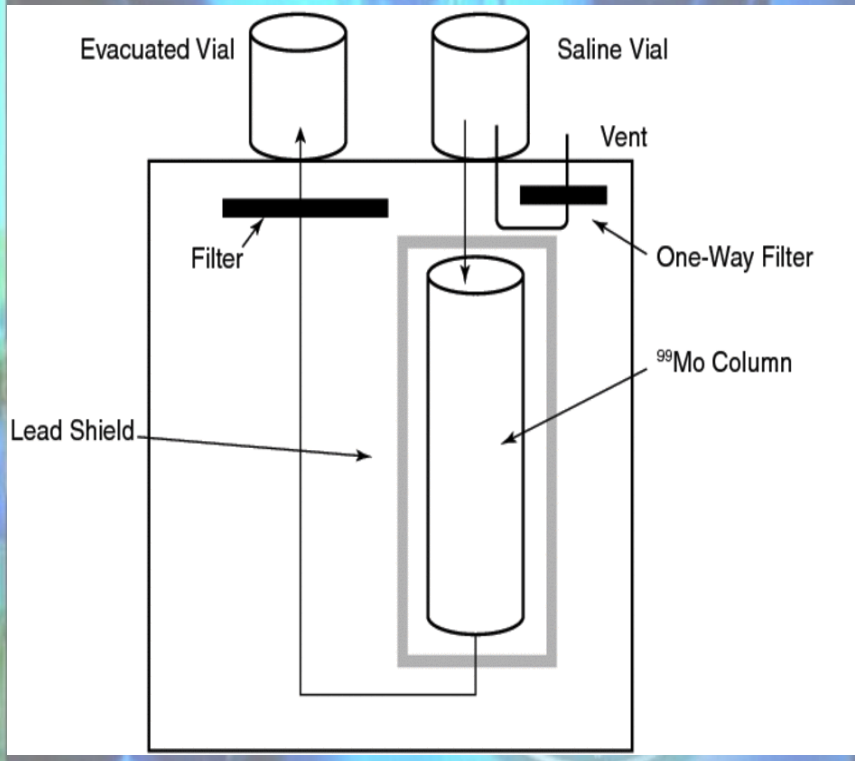




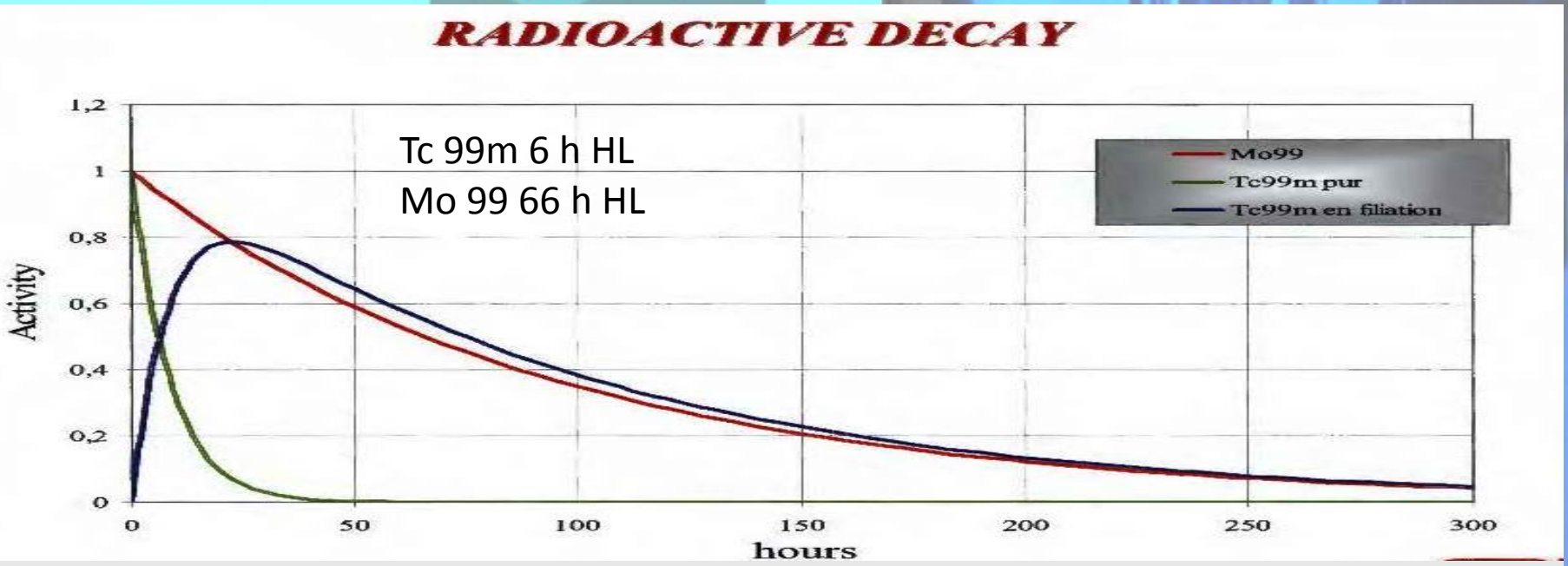
2nd time, 20 years later from fission products at the Brookhaven Graphite Research Reactor.

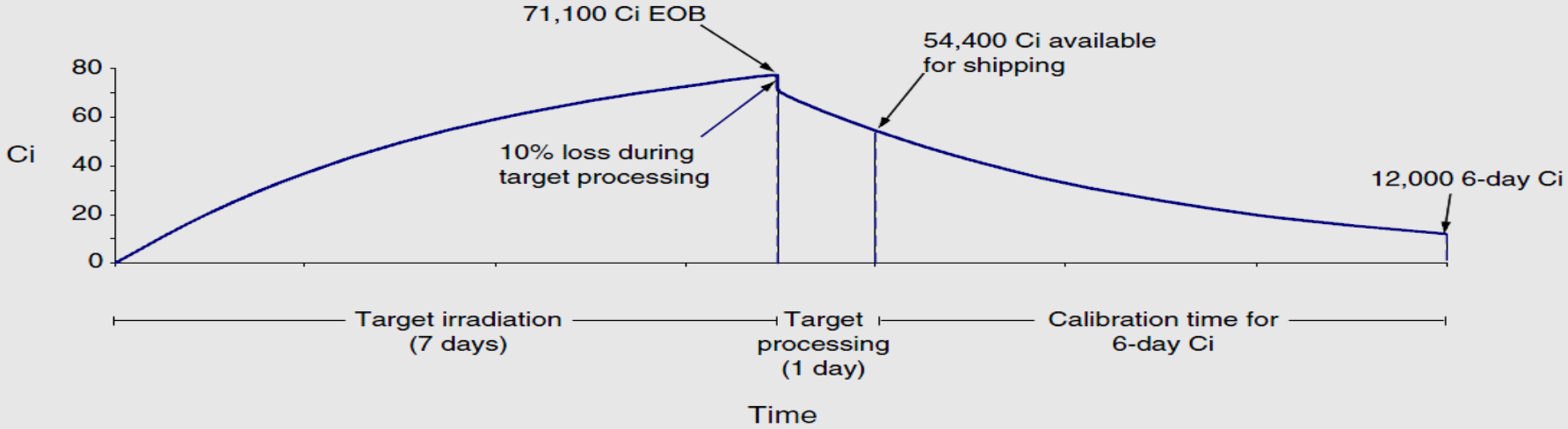
Conventional Method

- Indirect production
- Molybdenum 99 extracted from U235 fission products
- Tc 99m generators



The Time Factor

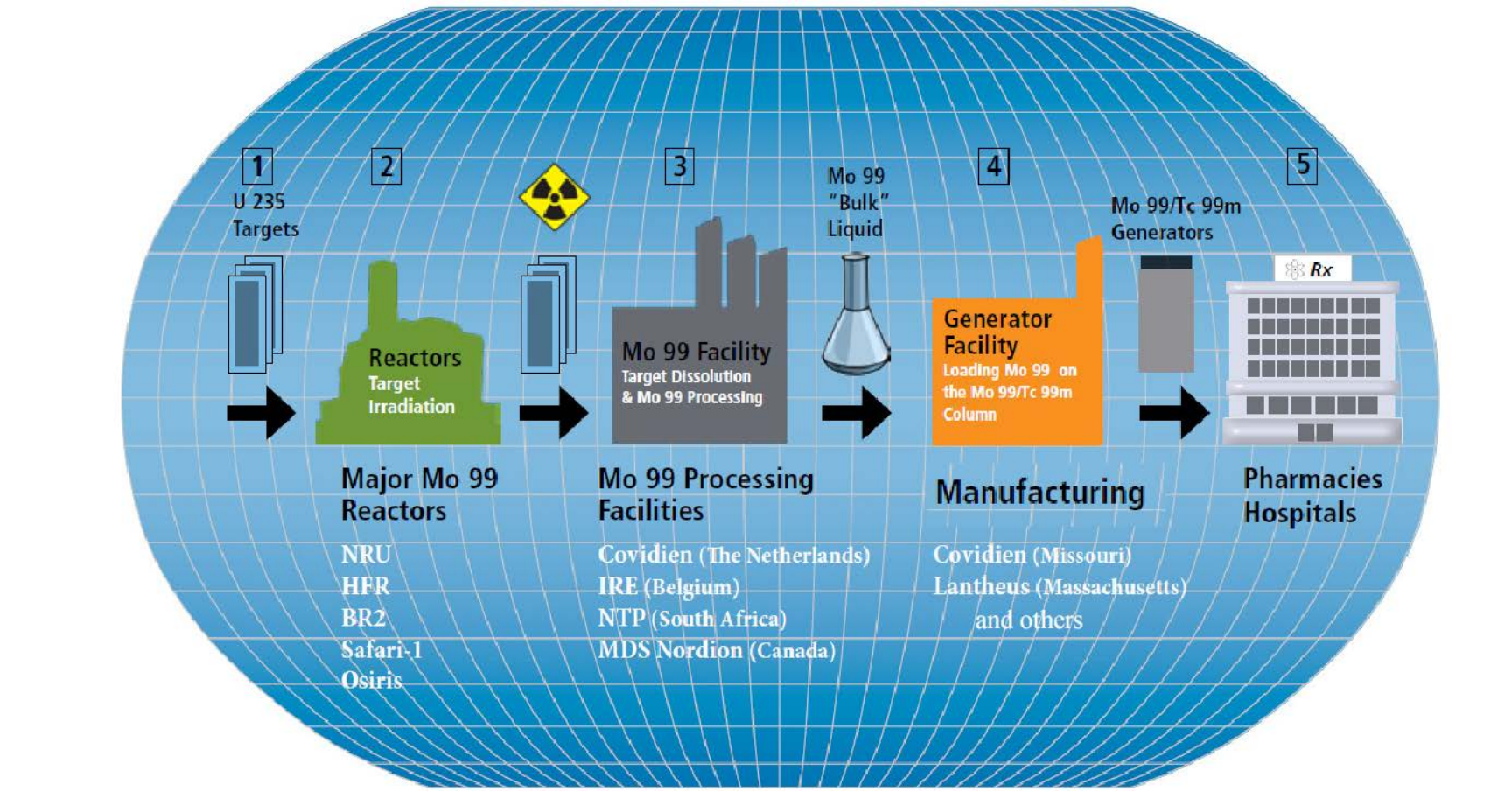




Canadian Moly, Chalk River

- Early experiments in the seventies by AECL
  - NRX reactor and processing at Tunney's Pasture labs in Ottawa
- Moly 99 Production Facility at Chalk River operational in 1984
- NRU + MPF became the world major source of moly (1/3 the world demand)
- Other supporting facilities at Chalk River: fuel fabrication and waste management

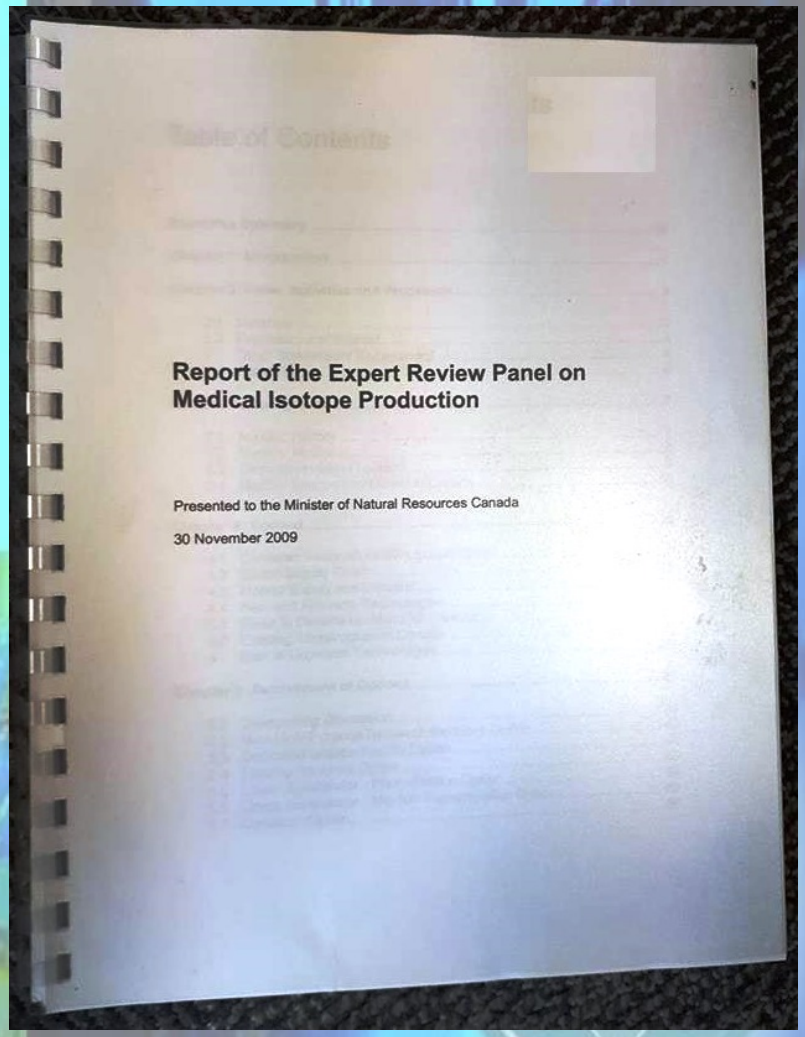
Global Supply Chain



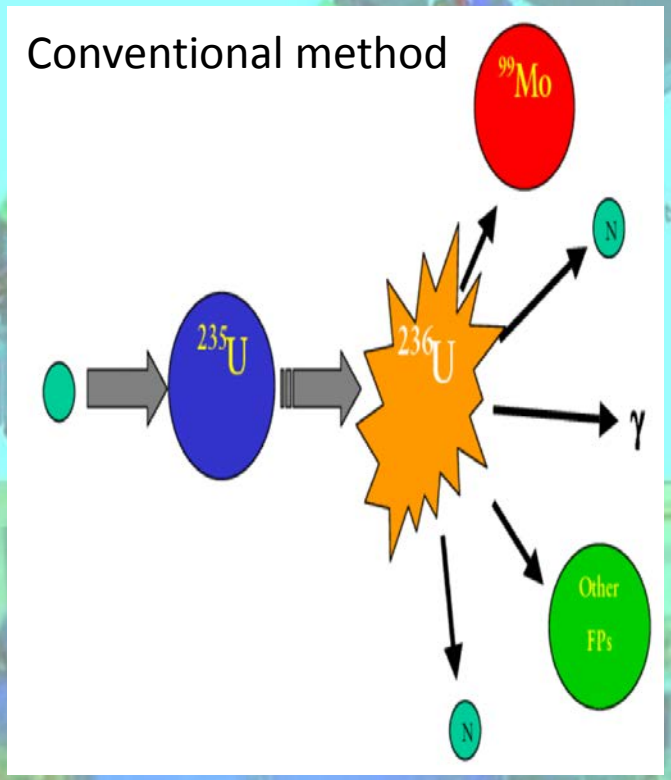
Source: covidien.com Oct 2009

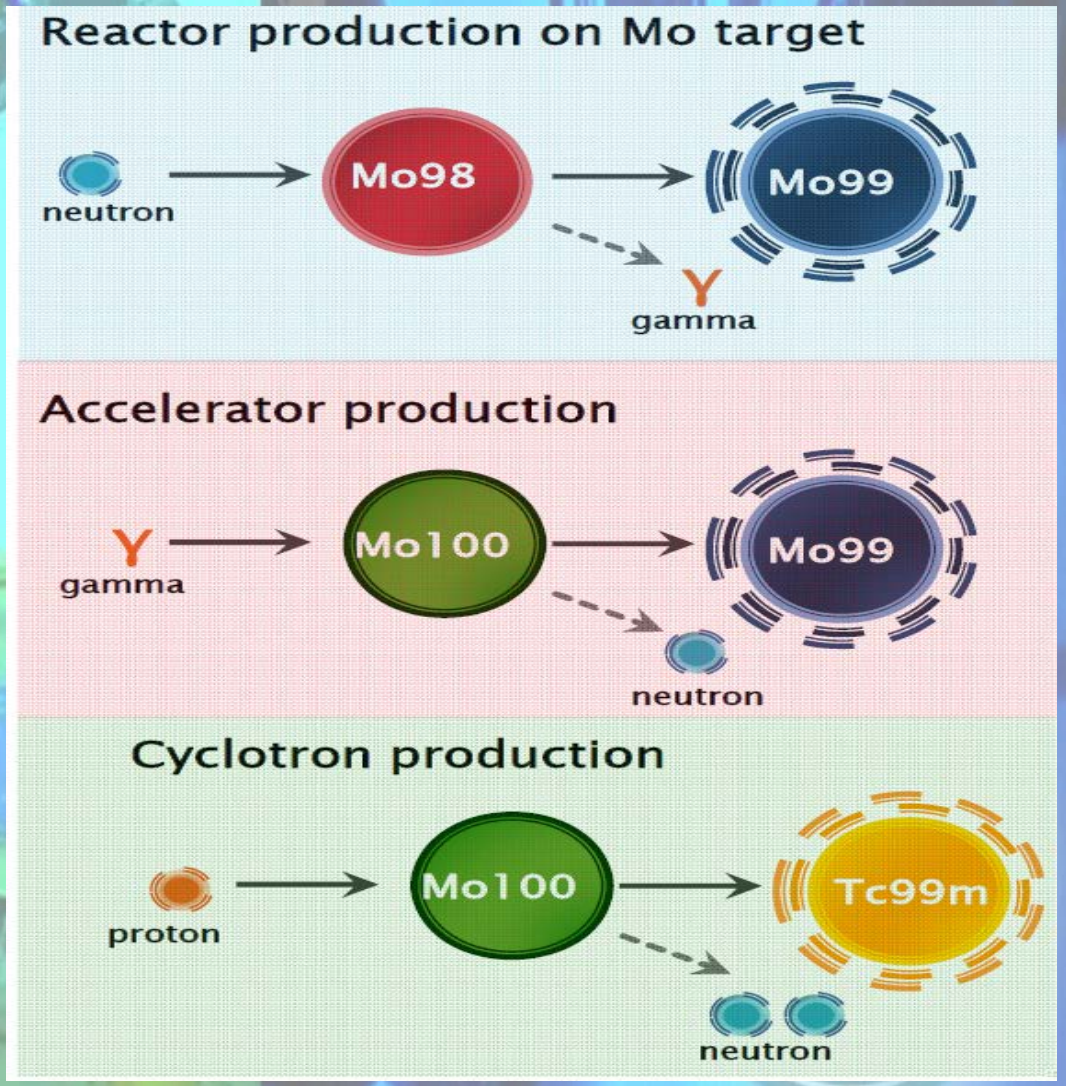
Isotope Crisis

- Unplanned shutdown of NRU
- Vulnerability of supply chain
- Expert Review Panel
- *To advise government on the most viable options for securing a predictable and reliable supply of Tc99m*



Alternative Methods





Six options assessed

1. New reactor
2. Existing reactor
3. DIF project
4. Cyclotron
5. Linear accelerator with Molybdenum
6. Linear accelerator with Uranium

Assessment Areas

raw materials	type
	cost/availability
	recycling required
irradiation	technology (reactor / accelerator)
	facility (commercial scale/demonstration)
targetry	target design available/requires R&D
	target station available/requires R&D
processing	technology proven / requires R&D
	Uranium based / Molybdenum based
	Facility requirements
	Facility availability
radioactive waste	whether it contains fissile materials or fission products
Technetium extraction	is generator required? Standard design available?
product	yield, capacity, proven or requires R&D
	pharmaceutical quality purity and specific activity
logistics	processing time, delivery and distribution range

Recommendations and Response

Main panel recommendations

- To support accelerator based solutions
- To move away from reactor based solutions
- Fission moly is not desirable
- To favor non government solutions

Main government responses

- Two R&D&D Funding Programs:
  - NISP (The Non-reactor-based Isotope Supply Contribution Program), 2010, $35m
  - ITAP (Isotope Technology Acceleration Program), 2012, $25 m

Proof of Principle

Cyclotron
Takács 2003

Evaluation of proton induced reactions on ^{100}Mo: New cross sections for production of ^{99m}Tc and ^{99}Mo

S. Takács, Z. Szücs, F. Tárkányi, A. Hermanne, M. Sonckz

Hungarian Academy of Sciences

Linacs
Bennett
1999

A System of ^{99m}Tc Production Based on Distributed Electron Accelerators and Thermal Separation

Ralph G. Bennett, Jerry D. Christian, David A. Petti, William K. Terry, S. Blaine Grover

Nuclear Technology / Volume 126 / Number 1 / April 1999 / Pages 102-121

Technical Paper / Radioisotopes

Path to Commercialization

- Irradiators
- Targetry
- Processing / Generators
- Target fabrication and recycling
- Product validation and medical approval
- Market

Radiopharmaceutical

- GMP
- Quality Control Tests
  - Biological
    - Sterility, toxicity, etc.
  - Physiochemical
    - pH
    - radionuclide purity
    - radiochemical purity
    - isotopic purity
    - chemical purity
- High specific activity, low dose, clear image, good bio-distribution

CNSC Regulatory Oversight

CNSC ahead of the game throughout the transition

- Conventional irradiation and processing facilities are under CNSC licences
- Licensing guide for accelerators revised to add clarity regarding isotope production
- Coordinated with and participated in gov. wide initiatives

CNSC Regulatory Oversight (continue)

- Certification of new Prescribed Equipments
- Licensing new facilities
- Amending existing licences to permit
  - Molybdenum irradiation
  - Target processing
  - Installation of new target systems and beamlines
- Compliance promotion

Safety and Control Areas

- Management system
- Human performance management
- Operating performance
- Physical design
- Fitness for service
- Radiation protection
- Conventional health and safety
- Environmental protection
- Emergency management and fire protection
- Waste management
- Security
- Safeguards and Non-Proliferation
- Packaging and transport

Current Licensed Facilities

Licensee	Location	Accelerator	Licence #	Mo Irradiation
Canadian Light Source Incorporated	Saskatoon, SK	MEVEX MB35-40	27107-5	Y
Alberta Health Services	Edmonton, AB	TR19	1832-100	N
Centre intégré universitaire de santé et de services sociaux de l'Estrie	Sherbrooke, QC	TR19, TR24	15453-7	Y
Sylvia Fedoruk Canadian Centre for Nuclear Innovation Inc.	Saskatoon, SK	TR24	15127-2	N
St. Joseph's Health Care	London, ON	GE PETtrace 16.5 MeV	13183-11	Y
McMaster University	Hamilton, ON	GE PETtrace 16.5 MeV	1495-16	N
U of Alberta	Edmonton, AB	TR24	6237-9	N
British Columbia Cancer Agency	Vancouver, BC	TR19	6074-101	Y
Thunder Bay Regional Health Sciences Centre	Thunder Bay, ON	TR24	1461-21	N
TRIUMF	Vancouver, BC	2 X TR30	PA1OL-01	Y

Progress toward Clinical Use

- 5 licensees reported irradiation of Mo100
- Clinical trials
  - underway in at least two centres
  - comparing Tc99m from accelerators with generators'Tc99m
  - using three kits (neutral, cationic, anionic)
  - Preliminary results successful with Technetium Pertechnetate

- New Drug Submission to Health Canada
  - Successful clinical trial results
  - Production procedure
  - Manufacturing site information
  - Quality control

Imaging Equipment in Canada

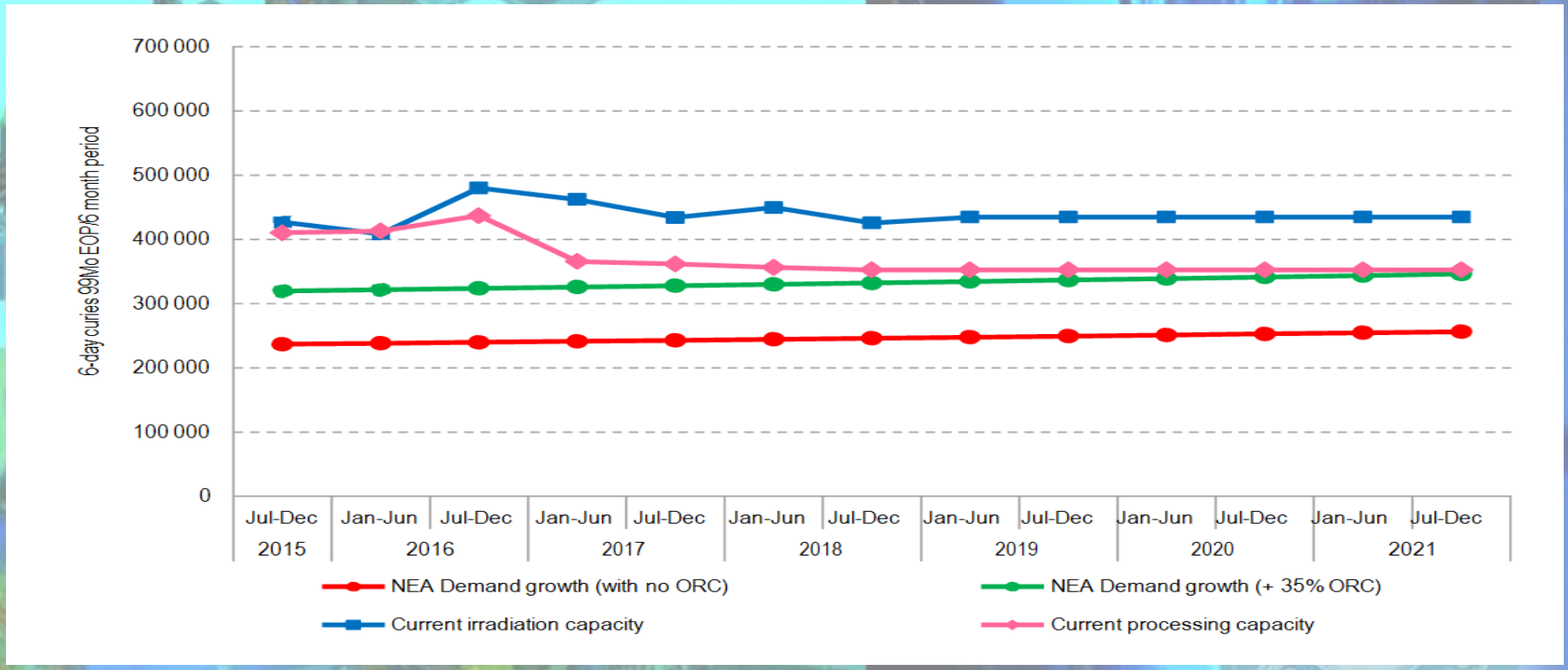
- Flattening growth in SPECT units
  - 264 in 2015
- More growth in SPECT-CT units
  - 39 additional units between 2012 and 2015
  - Total 214 in 2015
- No increase in demand of Tc99m

(source: The Canadian Medical Imaging Inventory, 2015, CADTH)

Imaging Equipment in Canada (cont.)

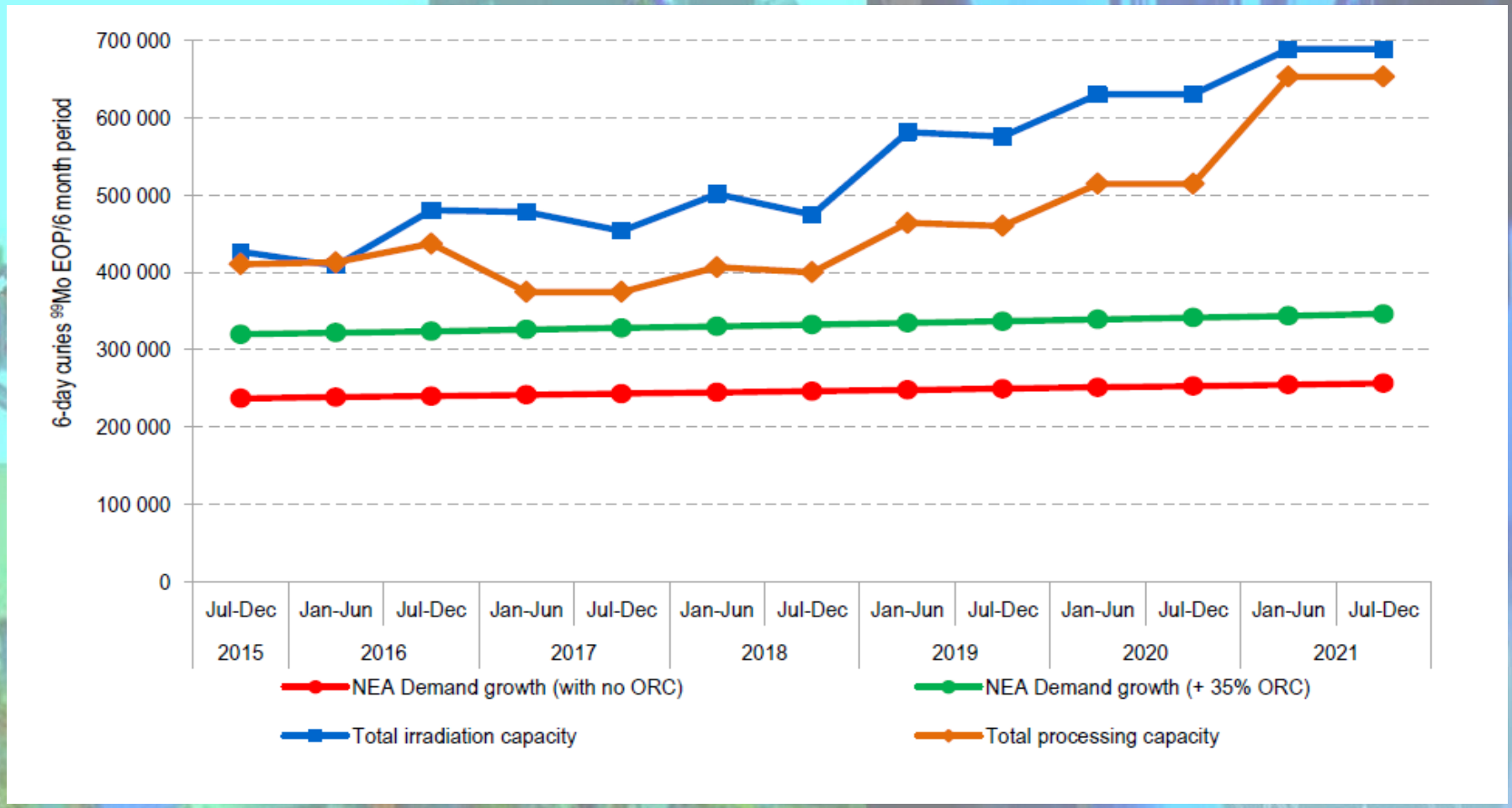
	Number of Units[a,b] (Number of Sites With Units)[c,b]					
Province	CT	MRI	SPECT	PET or PET-CT	PET-MRI	SPECT-CT
Alberta	50 (36)	41 (24)	30 (25)	4 (3)	0	35 (19)
British Columbia	65 (47)	42 (36)	26 (16)	3 (2)	0	27 (16)
Manitoba	19 (15)	10 (6)	7 (5)	1	0	8 (5)
New Brunswick	14 (10)	10 (9)	2 (2)	2 (2)	0	4 (4)
Newfoundland and Labrador	16 (14)	5 (5)	4 (2)	0	0	5 (3)
Northwest Territories	1	0	0	0	0	0
Nova Scotia	21 (16)	11 (10)	7 (4)	1	0	9 (8)
Nunavut	1	0	0	0	0	0
Ontario	186 (114)	125 (75)	99 (69)	15 (11)	2 (2)	38 (28)
Prince Edward Island	2 (2)	1	1	0	0	1 (1)
Quebec	146[d]	85[d]	79[e]	20 (20)	0	77[e]
Saskatchewan	16 (13)	9 (6)	9[f] (2)	1 (1)	0	10[f] (3[f])
Yukon	1 (1)	1	0	0	0	0
Canada	538 (305)	340 (216)	264 (130)	47 (39)	2 (2)	214 (91)

Demand and Supply Future



Source: NEA Report - March 2016 High-Level Group on the Security of Supply of Medical Radioisotopes

Better Scenario



Source: NEA Report - March 2016 High-Level Group on the Security of Supply of Medical Radioisotopes

Conclusion

- As the reactor based technetium 99m production is phased out in Canada new accelerator based production R &D &D is making significant progress
- The CNSC continues to perform its regulatory oversight and provide the regulatory clarity to help the emerging technologies reach its goals without compromising safety

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