3rd Workshop on Isotope Federal Supply and Demand

Global Concerns about Isotope Supply Chains

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International Atomic Energy Agency

Current Status of Radioisotope Uses and Trends

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Division of Physical and Chemical Sciences

Nuclear Physics

Accelerator applications

Nuclear Fusion

Research Reactor Applications

Nuclear Instrumentation

Radioisotope Products & Radiation Technology

Radiation Technology & Radiotracers

Radiopharmaceuticals – Development, Demonstration & Deployment

Nuclear Data

Data Bases

Development & Services

Nuclear Data

Atomic & Molecular Data

Isotope Hydrology

Hydrology Laboratory

Water resources management

Role of the IAEA & Areas of involvement

Mandate:

The Agency shall seek to accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world.

- Promote beneficial uses of radioisotopes and radiation technologies and assist MSs in these areas

Objectives

To contribute to improved healthcare and facilitate safe and clean industrial development in MS through the use of radioisotopes and radiation technology and to strengthen national capabilities for producing radioisotope products and utilizing radiation technology for socio-economic development

Section
Radioisotope Production and Radiation Technology

Rationale

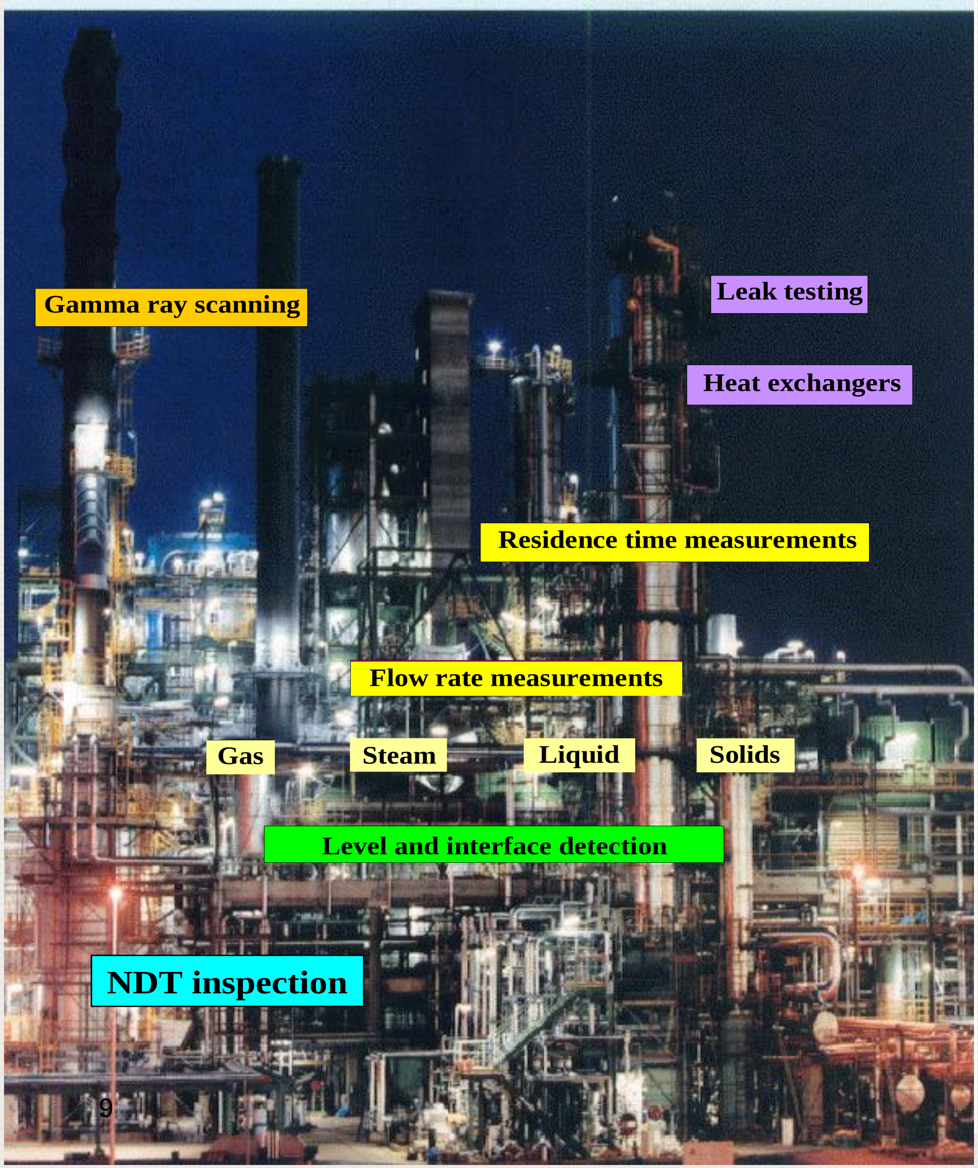
- Radioisotope products and radiation technology are the basic tools for nuclear applications in medicine, industry, agriculture, environment and allied research
- Demands for Agency’s support by Member States in developing local capability and infrastructure
- Need to foster emerging prospects for further applications
- Large number of on-going TC Projects (150).

Industrial Applications of Radiation Technology

- Radiotracers for process optimization
- Radiation based NDT for industrial applications – trouble shooting; process optimization
- Radiation Technology for clean environment
- Radiation Technology for novel materials
  - Nano materials for use in drug delivery (radiopharmaceuticals)
  - Bio-degradable, natural polymer based food packaging materials

Industrial Process control and safety
(radiotracers, sealed sources and nucleonic gauges)

- Enhance quality, productivity, reliability and safety
- Improve efficiency (Save Energy, Time & Money)
- Make worker's performance easier
- **Reduce industrial pollution**



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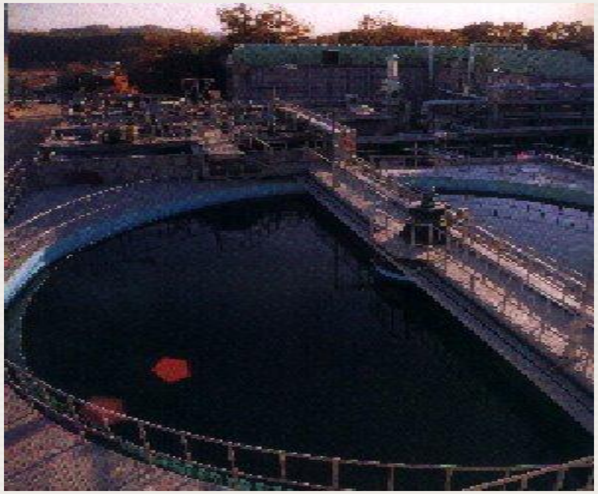
Radiation Processing Applications for Protection of the Environment

Flue gas Purification

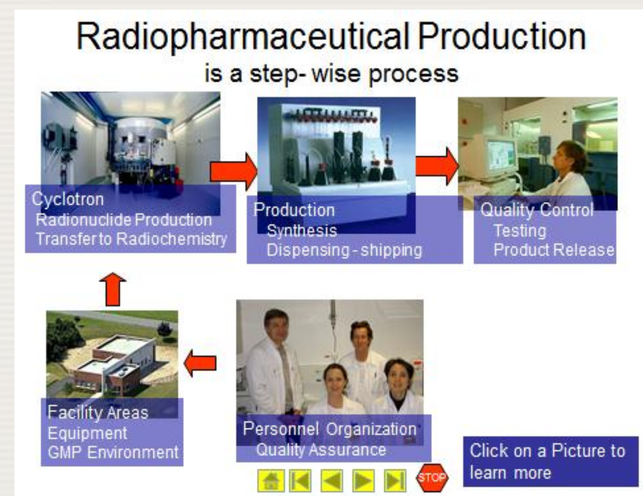


Wastewater Treatment

Sewage Sludge Hygienization

Radioisotopes and Radiopharmaceuticals

- Availing Medical Radioisotopes (Mo-99/Tc-99m; Ge-68/Ga-68; Y-90; Cu-64 etc.)
- Development of Radiopharmaceuticals (Lu-177-anti-CD20)
- Establishing production facilities – GMP/ regulatory compliant; training
- Updating radiopharmaceutical monographs for the International Pharmacopeia – WHO
- Preparation of syllabus for the Radiopharmacy courses in recognized Universities and e-learning modules for education and training in Radiopharmacy



Industrial Process control and safety
(radiotracers, sealed sources and nucleonic gauges)

Tracers for water

Isotope	^{137m}Ba	^{113m}In	^{99m}Tc	^{82}Br	^{198}Au
Half-life	2.6 min	100 min	6.02 hours	1.5 days	2.7 days
Energy (keV)	662	410	140	Approx. 700	410
Activity	1 to 200 mCi 37 to 7400 MBq	1 to 200 mCi 37 to 7400 MBq	1 mCi to 10 Ci 37 MBq to 370 GBq	1 to 200 mCi 37 to 7400 MBq	1 mCi to 9 Ci 37 MBq to 333 GBq
Obtention	Generator ^{137}Cs-^{137m}Ba	Generator ^{113}Sn-^{113m}In	Generator ^{99}Mo-^{99m}Tc	Reactor activation	Reactor activation
Preparation	None	EDTA Complexation	None	None	Complexation

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Industrial Process control and safety
(radiotracers, sealed sources and nucleonic gauges)

Tracers for liquid organic phase

Isotope	^{24}Na	^{82}Br	^{140}La	^{64}Cu	^{65}Ni
Half-life	2.58 years	1.5 days	1.7 days	12.84 hours	2.56 hours
Energy (keV)	1280	Approx. 700	330 to 1600	1340	370 to 1490
Chemical form	Naphtenate Salicylate	Bromobenzene	Naphtenate	Naphtenate	Stearate Oxalate
Isotope	^{198}Au	^{131}I	^{56}Mn	^{113m}In	^{60}Co
Half-life	2.7 days	8.05 days	4.58 hours	100 min	5.24 years
Energy (keV)	410	284 to 640	840 to 2110	390	1170 and 1330
Chemical form	Sodium cyanide solution	I-Kerosene Iodobenzene	Naphtenate	Oleate Stearate	Naphtenate

Industrial Process control and safety
(radiotracers, sealed sources and nucleonic gauges)

Tracers for gas phase

Isotope	^{41}Ar	^{76}As	^{82}Br	^{85}Kr	^{79}Kr	^{133}Xe	^{35}S
Half-life	110 min	26.5 h	36 h	10.6 a	34 h	5.27 d	87 d
Energy (keV)	1370	550 to 2020	550 to 1320	β^- 540 to 700	136 to 830	β^- 30 to 340	β 167
Chemical form	Gas	AsH_3	CH_3Br	Gas	Gas	Gas	H_2S

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Industrial Process control and safety
(radiotracers, sealed sources and nucleonic gauges)

Tracers for sand particles

Isotope	^{140}La	^{198}Au	^{52}Mn	^{147}Nd	^{192}Ir
Half-life	1.7 days	2.7 days	5.7 days	11 days	74 days
Energy (keV)	330 to 1600	410	730 to 1460	Complex spectrum	296 to 468
Activity	< 0.5 Ci < 18 GBq	< 9 Ci < 333 GBq	< 0.5 Ci < 18 GBq	< 3 Ci < 111 GBq	< 1 Ci < 37 GBq
Obtention	Reactor activation	Reactor activation	Reactor activation	Reactor activation	Reactor activation
Preparation	Glass powder	Glass powder	Glass powder	Glass powder	Glass powder

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Industrial Process control and safety
(radiotracers, sealed sources and nucleonic gauges)

Tracers for mud/sludge particles

Isotope	^{113m}In	^{99m}Tc	^{198}Au	^{51}Cr	$^{175+181}Hf$	^{160}Tb	^{46}Sc
Half-life	100 min	6.02 hours	2.7 days	27 days	45 days	73 days	84 days
Energy (keV)	390	140	410	320	Complex spectrum	Complex spectrum	900 and 1100
Activity	< 200 mCi < 7.40 GBq	< 10 Ci < 370 GBq	< 9 Ci < 333GBq	< 20 Ci < 740 GBq	< 1 Ci < 37 GBq	< 1 Ci < 37 GBq	< 9 Ci < 333 GBq
Obtention	Generator ^{113}Sn–^{113m}In	Generator ^{99}Mo-^{99m}Tc	Reactor activation	Reactor activation	Reactor activation	Reactor activation	Reactor activation
Preparation	None	Particles in reducing medium	Chloride solution $HAuCl_4^-$	Chloride solution	Chloride solution	Chloride solution	Chloride solution

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Industrial Process control and safety
(radiotracers, sealed sources and nucleonic gauges)

Sealed sources for gauges

Isotope	^{60}Co	^{137}Cs	^{241}Am	^{241}Am-Be	^{252}Cf
Half-life	5.271 years	30.1 years	432 years	432 years	2.6 years
Energy	1.17 MeV 1.33 Mev	662 keV	60 keV	Neutrons 2 – 10 MeV	Neutrons 2 MeV
Activity	< 200 mCi < 7.4 GBq	< 200 mCi < 7.4 GBq	< 1 Ci < 37 GBq	< 10 Ci < 370 GBq	

Sealed sources for NDT

Isotope	^{60}Co	^{75}Se	^{192}Ir
Half-life	5.271 years	120 days	74 days
Energy	1.17 MeV 1.33 MeV	120 to 400 keV	296 to 468 keV
Activity	< 50 Ci < 1850 GBq	< 100 Ci < 3700 GBq	< 100 Ci < 3700 GBq

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Industrial Process control and safety
(radiotracers, sealed sources and nucleonic gauges)

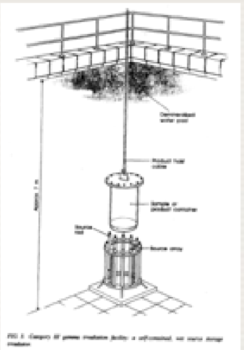
Main issues

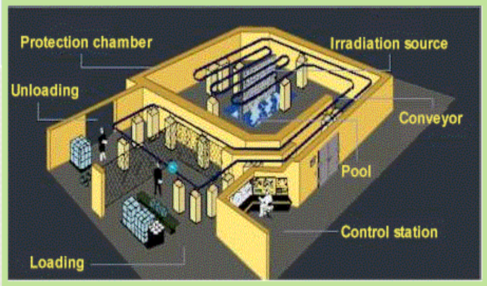
- Reactor time for irradiation
- Some generators have been discontinued
- Price of the generators

Cobalt-60 irradiators for different applications

$$^{59}\mathrm{Co}(n,\gamma)^{60}\mathrm{Co}$$

S.No.	Type	Typical Cobalt-60 Source strength (Curie)	Application area
1	Gamma Cell with irradiation volume of 1-5 litres	1,000-20,000	R&D at laboratory scale Blood irradiation Irradiation of seeds etc. for mutation breeding
2	Panoramic Batch Irradiators	30,000-100,000	Pilot scale studies Semi-commercial operations for sterilization of medical products Food irradiation requiring low dose irradiation such as irradiation of onions, potatoes, mangoes etc.
3	Commercial Gamma radiation plants	100,000-5,000,000	Sterilization of medical products Food irradiation requiring high doses such as hygienization of spices





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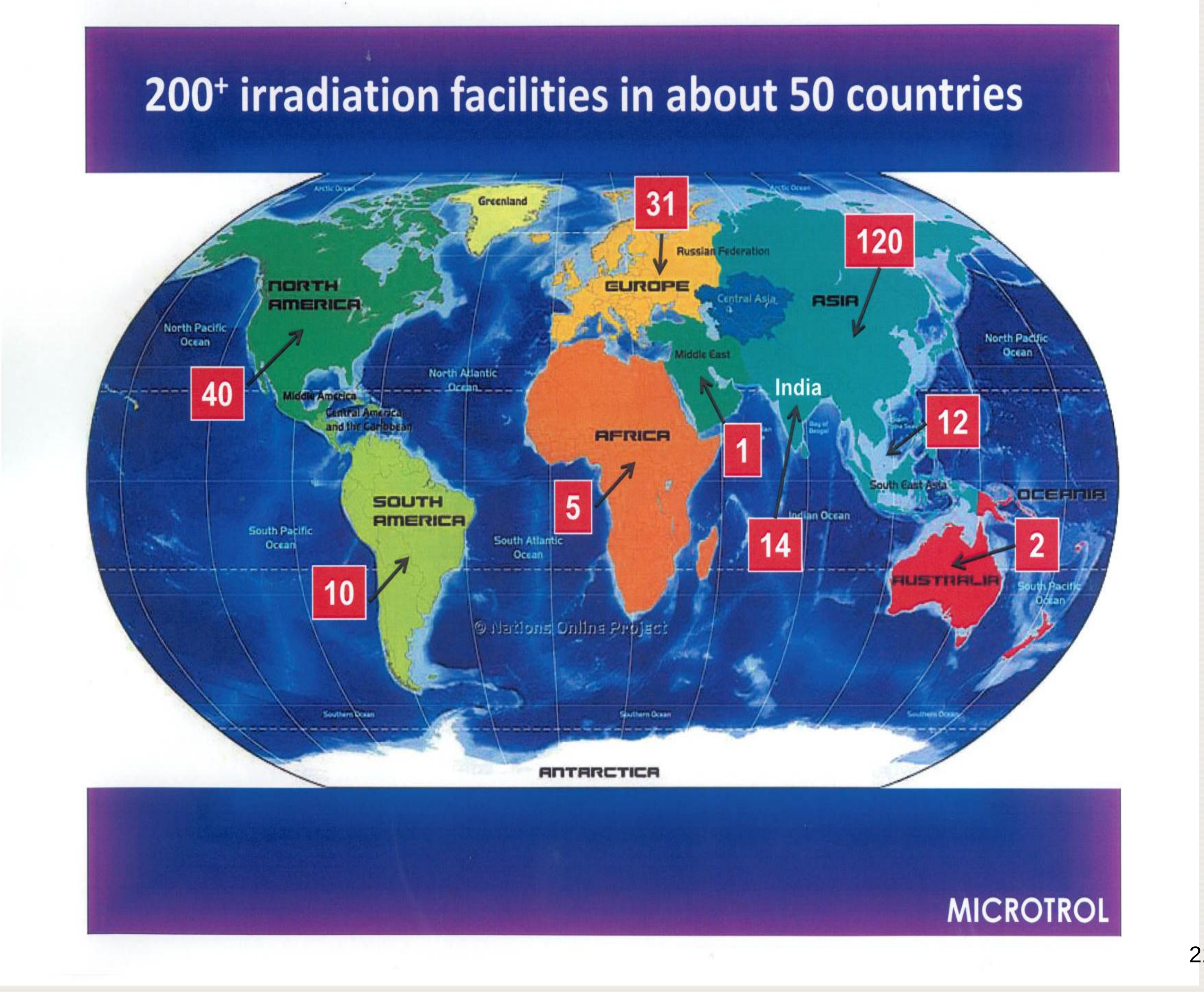
Development of gamma irradiation

- First commercial plant built in early 1960s
- Over 800 million Ci of Co-60 shipped over last 50 years
- Today about 300 million Ci of Co-60 worldwide
- Ca. 145 million Ci of Co-60 installed in about 50 gamma facilities in the US
- About 12 million m^3 of single use medical devices sterilized by radiation annually.

Cobalt-60 irradiators for different applications

133 facilities in 41 countries in 1985



Issues regarding supply of Cobalt-60

- > 200 commercial irradiation facilities in the world (medical sterilization and food irradiation) > 260 M Ci.
- Growth rate of 5-10% and the decay rate of 12% per annum: annual demand of Co-60 is about 50 M Ci.
- The current supply of Co-60 meets the demand and IAEA has been able to procure and ensure the supply for some Member States, though the transportation across the continents poses a few challenges
- Co-60 is produced in CANDU and RBMK power reactors in Canada, Russia, China, Argentina and India. CANDU reactors have a 25-year life span and much of the installed reactors will reach this milestone over the next decade.
- Many CANDUs are being refurbished extending their life by an additional 25-30 years.
- Canada, major distributor of Co-60 using multiple reactor, may face distribution issues in the near future.

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Radioisotopes for Medicine

Teletherapy

Isotope	^{60}Co	^{137}Cs
Half-life	5.271 years	30.1 years
Energy	1.17 MeV 1.33 MeV	662 keV
Activity	< 13,000 Ci < 500 TBq	
Production	$^{59}Co(n,\gamma)^{60}Co$	Fission product

Radioisotopes for Medicine

Braquitherapy

Isotope	^{192}Ir	^{125}I	^{103}Pd
Half-life	74 days	60 days	74 days
Photon average energy	380 keV	28 keV	21 keV
Production	$^{191}Ir(n,\gamma)^{192}Ir$	$^{124}Xe(n,\gamma)^{125}Xe$ $^{125}Xe \rightarrow {}^{125}I$ Enriched target	$^{102}Pd(n,\gamma)^{103}Pd$ Enriched target $^{103}Rh(p,n)^{103}Pd$

Brachytherapy classification with respect to dose rate:

- Low dose rate (LDR) (0.4 – 2 Gy/h)
- Medium dose rate (MDR) (2 – 12 Gy/h)
- High dose rate (HDR) (> 12 Gy/h) < 10 Ci/pellet

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Radioisotopes for Nuclear Medicine - Diagnostic

PET (Cyclotron)

Isotope	^{11}C	^{13}N	^{15}O	^{18}F
Half-life	20 min	10 min	2 min	110 min
Production	$^{14}N(p,\alpha)^{11}C$	$^{16}O(p,\alpha)^{13}N$	$^{15}N(p,n)^{15}O$	$^{18}O(p,n)^{18}F$ enriched

Isotope	^{64}Cu	^{68}Ga	^{82}Rb	^{89}Zr
Half-life	12.7 h	68 min	1.25 min	78.4 h
Production	$^{64}Ni(p,n)^{64}Cu$ enriched	Generator (^{68}Ge-^{68}Ga) $^{nat}Ga(p,xn)^{68}Ge$ High energy Cyclotron	Generator (^{82}Sr-^{82}Rb) $^{85}Rb(p,4n)^{82}Sr$ High energy Cyclotron	$^{89}Y(p,n)^{89}Zr$

Radioisotopes for Nuclear Medicine - Diagnostic

SPECT

Isotope	^{67}Ga	^{99m}Tc	^{111}In	^{123}I	^{201}Tl
Half-life	78.3 h	6 h	67.2 h	13 h	73 h
Production	$^{68}Zn(p,2n)^{67}Ga$ enriched	Generator (^{99}Mo-^{99m}Tc)	$^{112}Cd(p,2n)^{111}In$ enriched	$^{124}Xe(p,2n)^{123}Cs$ $^{123}Cs \rightarrow {}^{123}Xe \rightarrow {}^{123}I$ enriched	$^{203}Tl(p,3n)^{201}Pb$ $^{201}Pb \rightarrow {}^{201}Tl$ enriched

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Radioisotopes for Nuclear Medicine - Therapy

B^- emitters

Isotope	^{32}P	^{90}Y	^{153}Sm	^{131}I	^{177}Lu
Half-life	14.3 d	2.7 d	46.3 h	8 d	6.7 d
Production	$^{32}S(n,p)^{32}P$	Generator (^{90}Sr-^{90}Y) $^{89}Y(n,\gamma)^{90}Y$ Fission product	$^{152}Sm(n,\gamma)^{153}Sm$ enriched	$^{130}Te(n,\gamma)^{131}Te$ $^{131}Te \rightarrow {}^{131}I$ Fission product	$^{176}Lu(n,\gamma)^{177}Lu$ $^{176}Yb(n,\gamma)^{177}Yb$ $^{177}Yb \rightarrow {}^{177}Lu$ enriched

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Radioisotopes for Nuclear Medicine - Therapy

α emitters

Isotope	Half-life	Production	Production
^{225}Ac	10 d	^{233}U decay chain ^{229}Th(α decay)	$^{226}Ra(p,2n)^{225}Ac$
^{224}Ra	3.66 d	^{228}Th(α decay)	
^{223}Ra	11.4 d	^{227}Ac decay chain ^{227}Th(α decay)	$^{226}Ra(n,\gamma)^{227}Ac$
^{213}Bi	45.6 min	^{227}Ac decay chain	Ac-Bi generator
^{212}Bi	60 min	^{227}Ac decay chain	Ra-Bi/Pb generator
^{211}At	7.2 h		$^{209}Bi(\alpha,2n)^{211}At$

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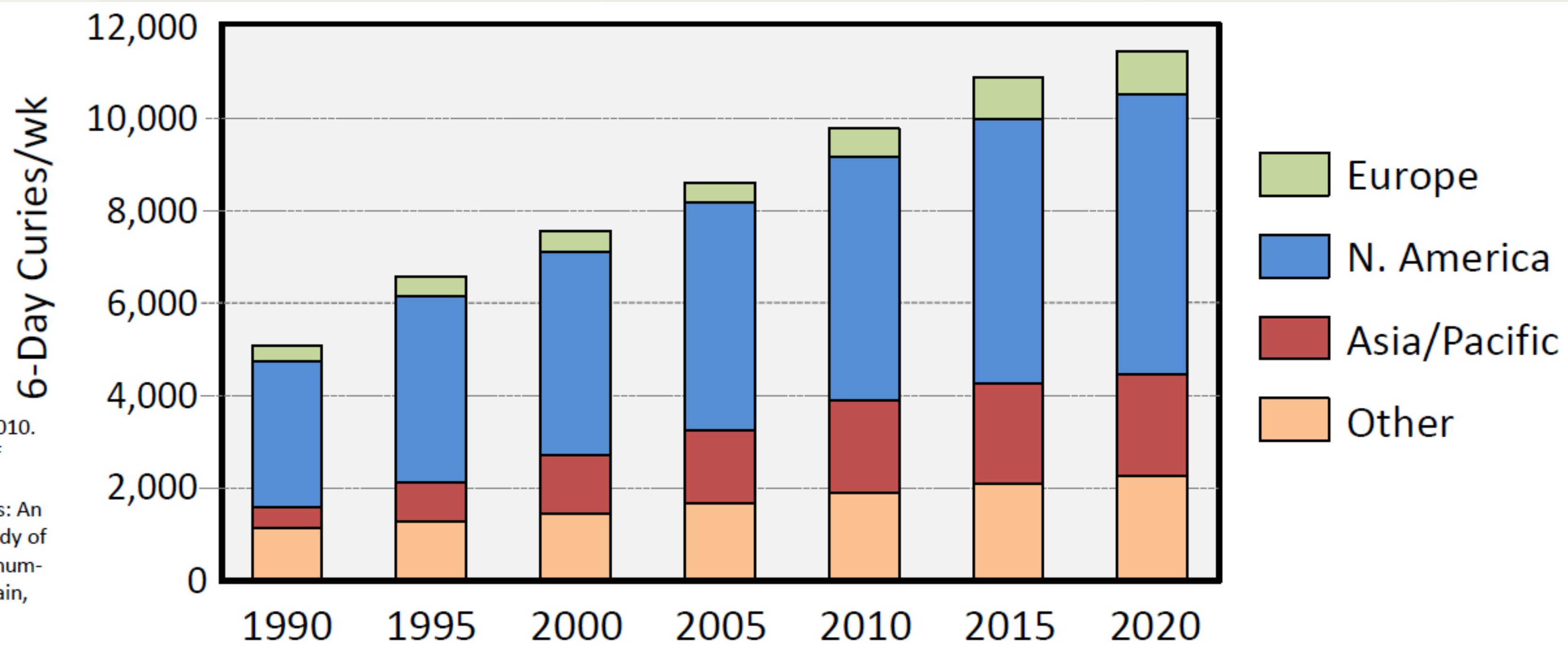
Radioisotopes for Nuclear Medicine - Therapy

Issues

- I-131 supply could be affected by Mo-99 crisis
- The only alpha emitter radiopharmaceutical, Xofigo, had its distribution temporarily suspended due to a chemical processing issue
- Enriched targets of Lu-176 and/or Yb-176
- Potential new β^- emitters: Cu-67, Re-186, Sc-47
- Theranostic

Demand of Mo-99

- 10,000 6-day Ci per week (world)
- 5,000 6-day Ci per week (USA)



OECD-NEA, 2010. The Supply of Medical Radioisotopes: An Economic Study of the Molybdenum-99 Supply Chain, NEA 6967.

Fission

- ***Producers Mo-99***
  - ***Mallinckrodt (USA/Holland)***
  - ***IRE (Belgium)***
  - ***Nordion (Canada)***
  - ***Russia***
  - ***NTP (South Africa)***
  - ***ANSTO (Australia)***
  - ***Argentina***

HEU

HEU/LEU

LEU

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Supply of Mo-99 crisis

- Supply problems since 2007
- Main shortage in 2009
- Ageing of Reactors
- 2014: latest problem NTP
- 2016: Nordion will cease production

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IAEA Priorities for ^{99}Mo

HEU Minimization

Transition of ^{99}Mo production away from the use of highly enriched uranium (HEU)

Stability of Supply

Diversification of supply and movement to full cost recovery to ensure the global demand is met

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Role of IAEA

- Stability of supply of Mo-99 in MSs
- Indigenous production using non-HEU targets:
  - $^{235}U(n,f)^{99}Mo$ reaction
  - $^{98}Mo(n,\gamma)^{99}Mo$ reaction
  - $^{100}Mo(p,2n)^{99m}Tc$ reaction Cyclotron
- Regulatory aspects
- New alternatives to Tc-99m
- To assist MSs to improve operational performance / reliability of an ageing fleet of RRs
- Efforts from NEFW and RPRT sections

Small-scale, non-HEU ^{99}Mo production

- TC (INT) Project started in 2013
- Aimed at assisting small-scale, national-level producers in setting up their production capability;
  - NOT aimed at creating commercial producers
- Will rely on LEU fission or n,gamma-based production
- Open to any IAEA Member States wishing to receive advice and assistance
- Production infrastructure fact-finding missions (experts) were completed to Mexico, Morocco, Peru, Poland and Romania. Similar missions were conducted in Egypt (2010) and Malaysia (2011)

Role of RPRT

- CRP on the production of Tc-99m by cyclotron (3rd RCM 2015)
- CT on The Preparation of Monograph of Tc-99m Produced by Cyclotron (2015)
- TM on New Ways of Producing Tc-99m and Tc-99m Generators (2015)
- New CRP on "Sharing and Developing Protocols to Further Minimize Radioactive Gaseous Releases to the Environment in the Manufacture of Medical Radioisotopes, as Good Manufacturing Practice”
- Support to TC projects

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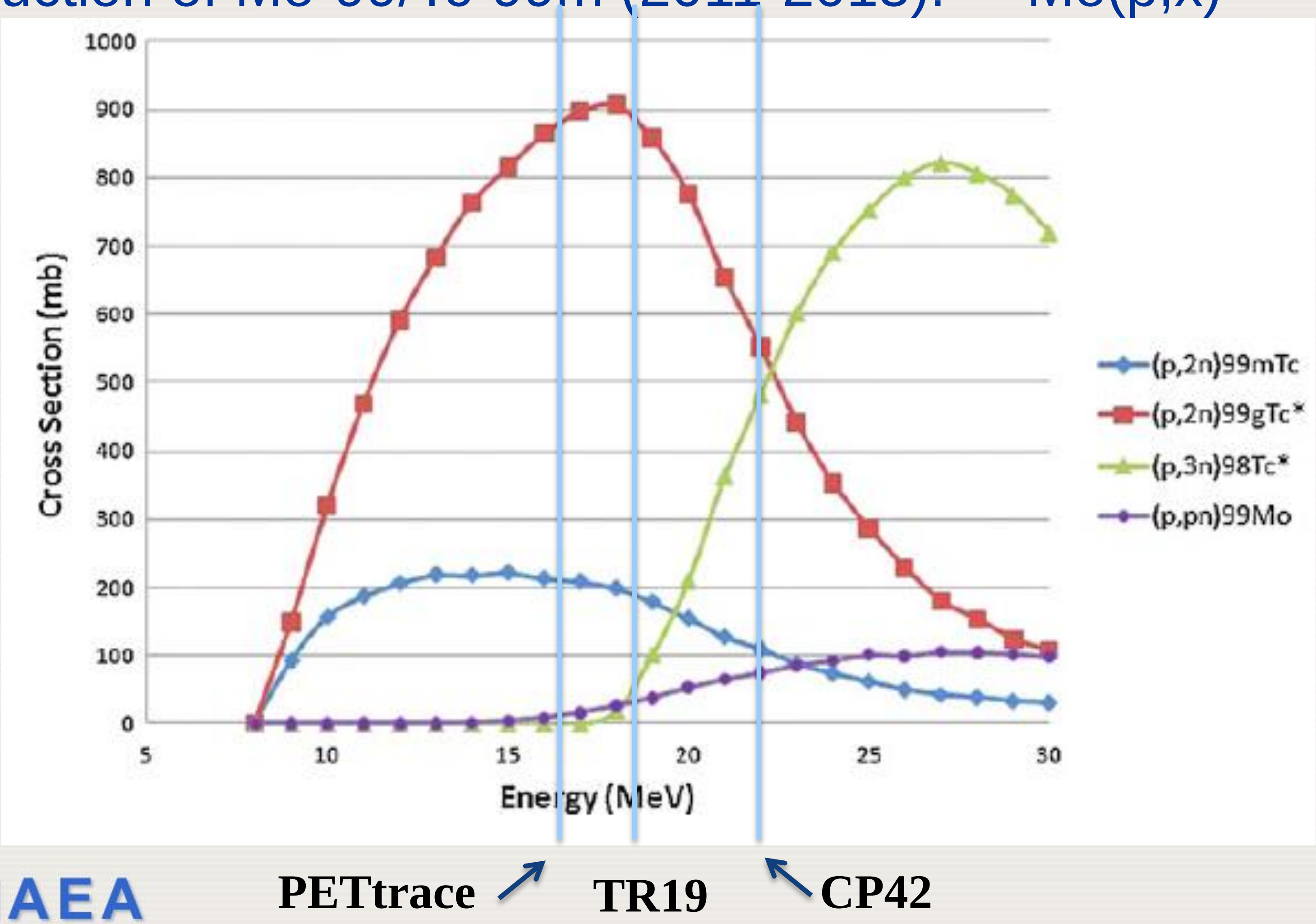
Production of ^{99m}Tc in Cyclotron

IAEA CRP - Accelerator-based Alternatives to Non-HEU production of Mo-99/Tc-99m (2011-2015): ^{100}Mo(p,x)



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A. Celler, X. Hou, F. Bénard, T. Ruth, Phys. Med. Biol. 2011, 56, 5469

Role of RPRT

- Alternatives for Tc-99m: Tl-201, Rb-82, F-18-Fluoride, Ga-68, Cu-64
- CRPs on:
  - F-18 radiopharmaceuticals
  - Ga-68 radiopharmaceuticals
  - Production of Cu-64 and I-124

Important Issue for Mo-99

- Promising alternatives for production of Mo-99/Tc-99m use enriched Mo-98 or Mo-100 targets
- Only one supplier in the world

THANK YOU FOR YOUR KIND ATTENTION!

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