Equivalence and Comparisons for Nuclides of Interest to Medicine

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Workshop on Standards and Measurements for Alpha Emitting Nuclides in Therapeutic Nuclear Medicine, 22nd February 2024

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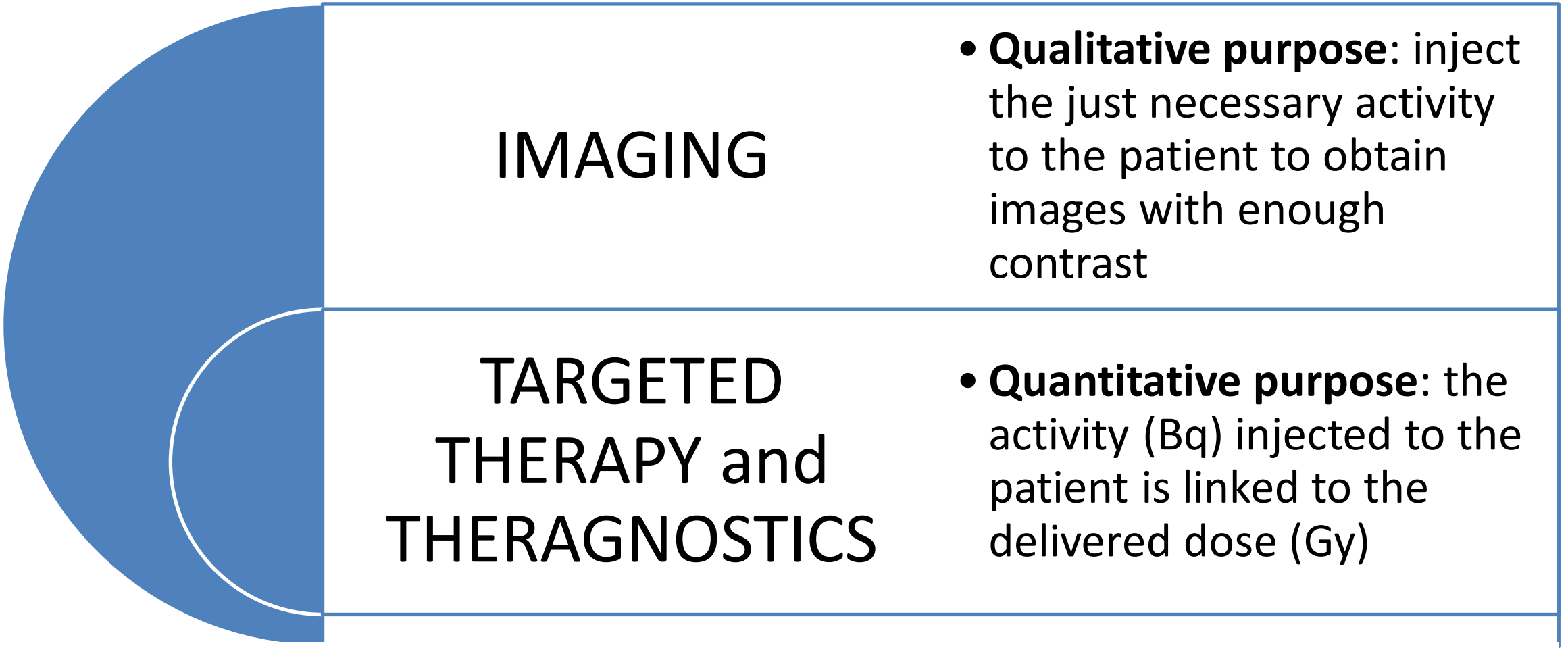
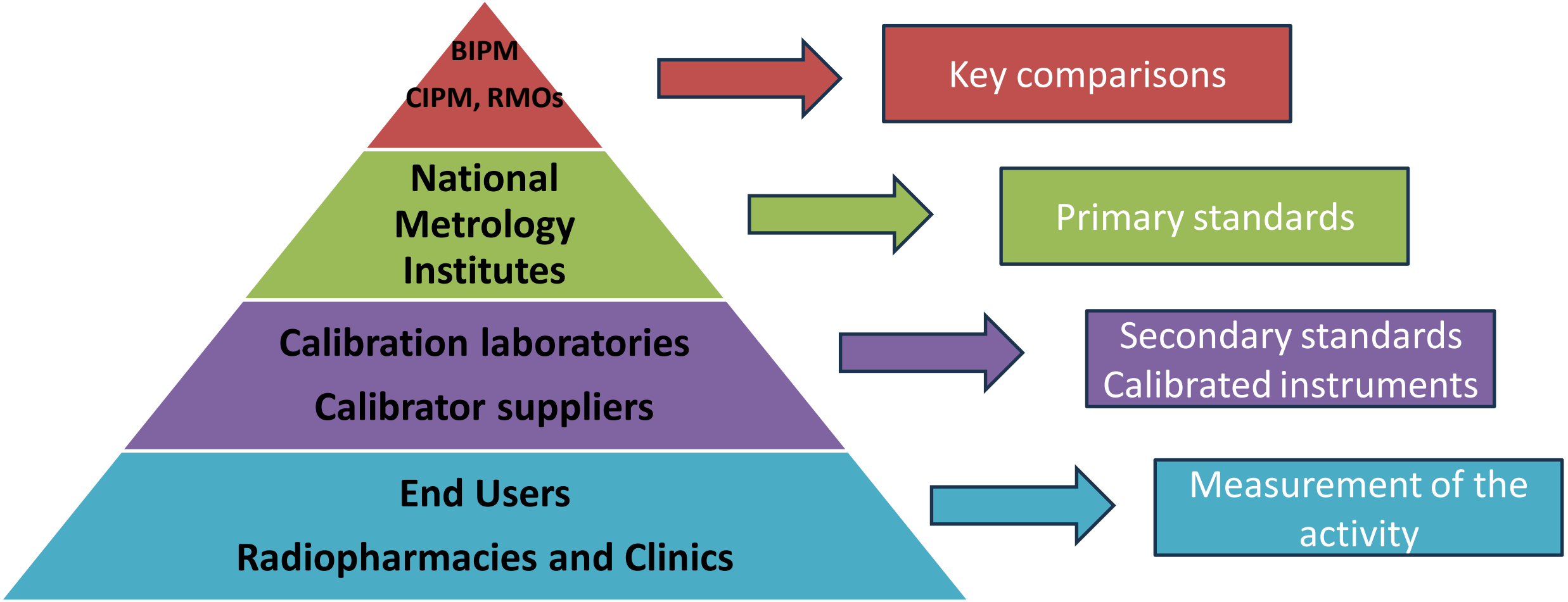
Part 1. Context and international equivalence of the Bq

Metrology in nuclear medicine



Increased importance of metrological traceability to the derived SI unit: the becquerel (Bq)

The traceability chain to the SI derived unit, the becquerel (Bq)



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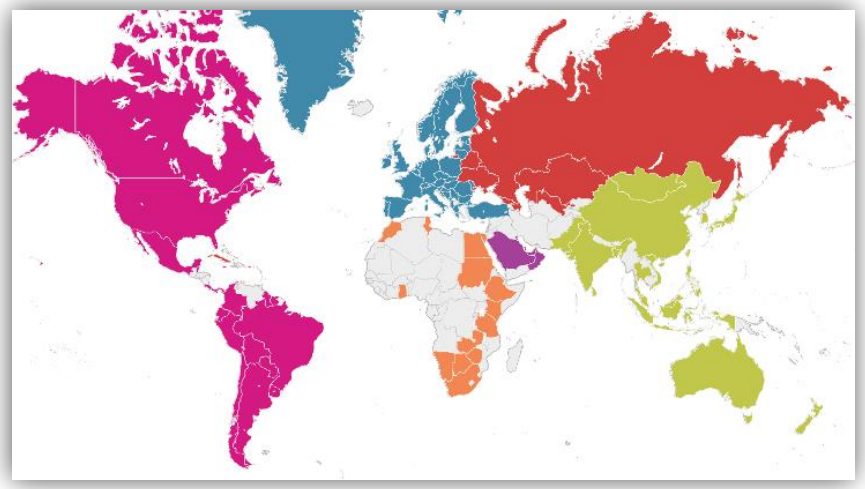
Calibration and Measurement Capabilities (CMCs) and Key Comparisons (KCs)

- **CIPM Mutual Recognition Arrangement (CIPM MRA) - 1999**
  - To demonstrate the international equivalence of measurement standards
  - 250 institutes (97 NMIs, 4 IOs, 149 DIs)
  - Key Comparisons (KCs) is a way to assess the international equivalence of measurement standards
  - **Calibration and Measurement Capabilities (CMCs)** published by the KCDB

https://www.bipm.org/kcdb/



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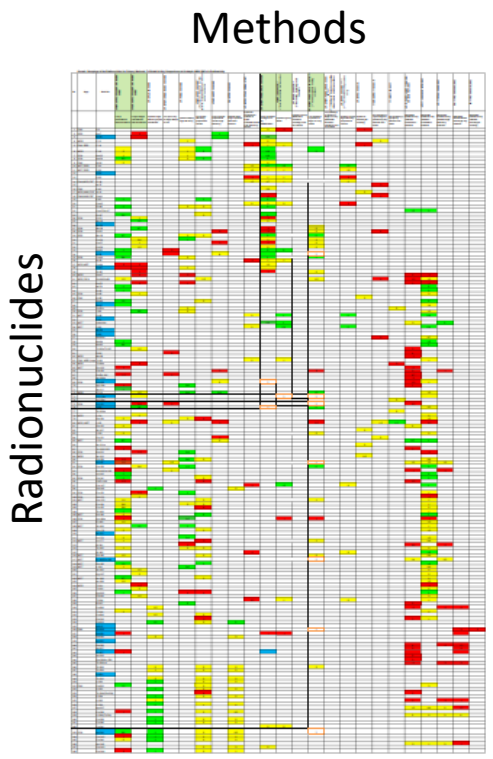
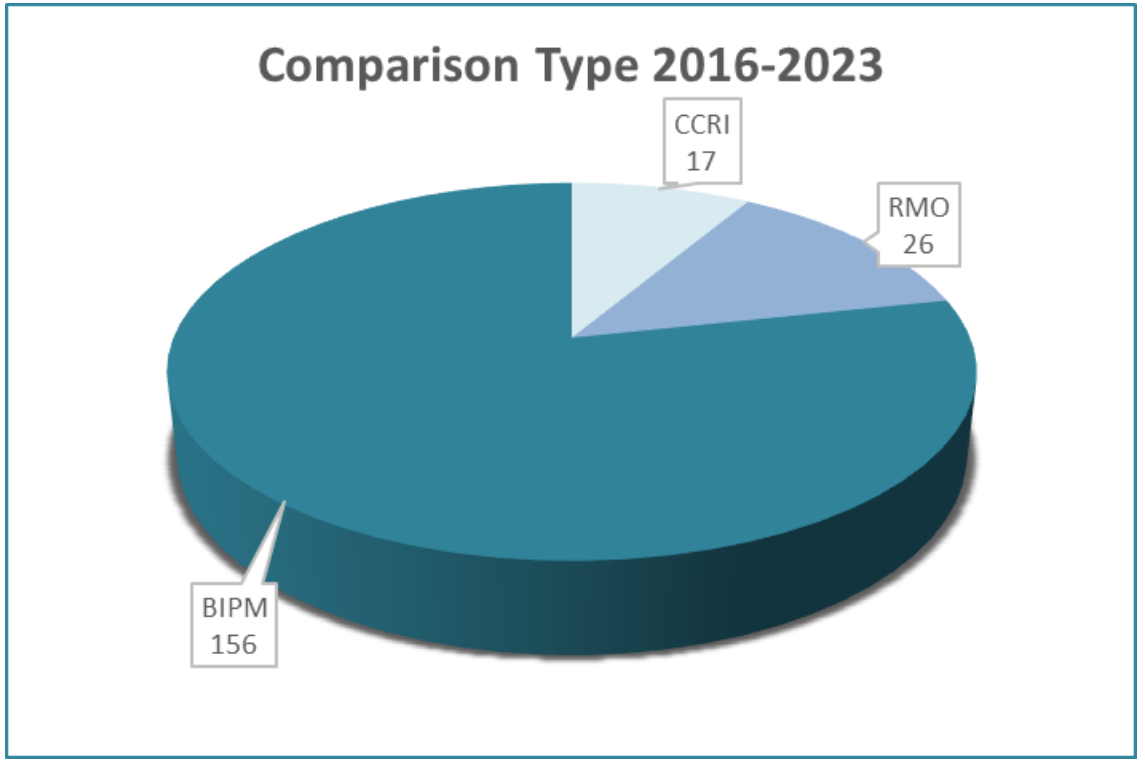
In radionuclide metrology, the support of CMCs by Key Comparison

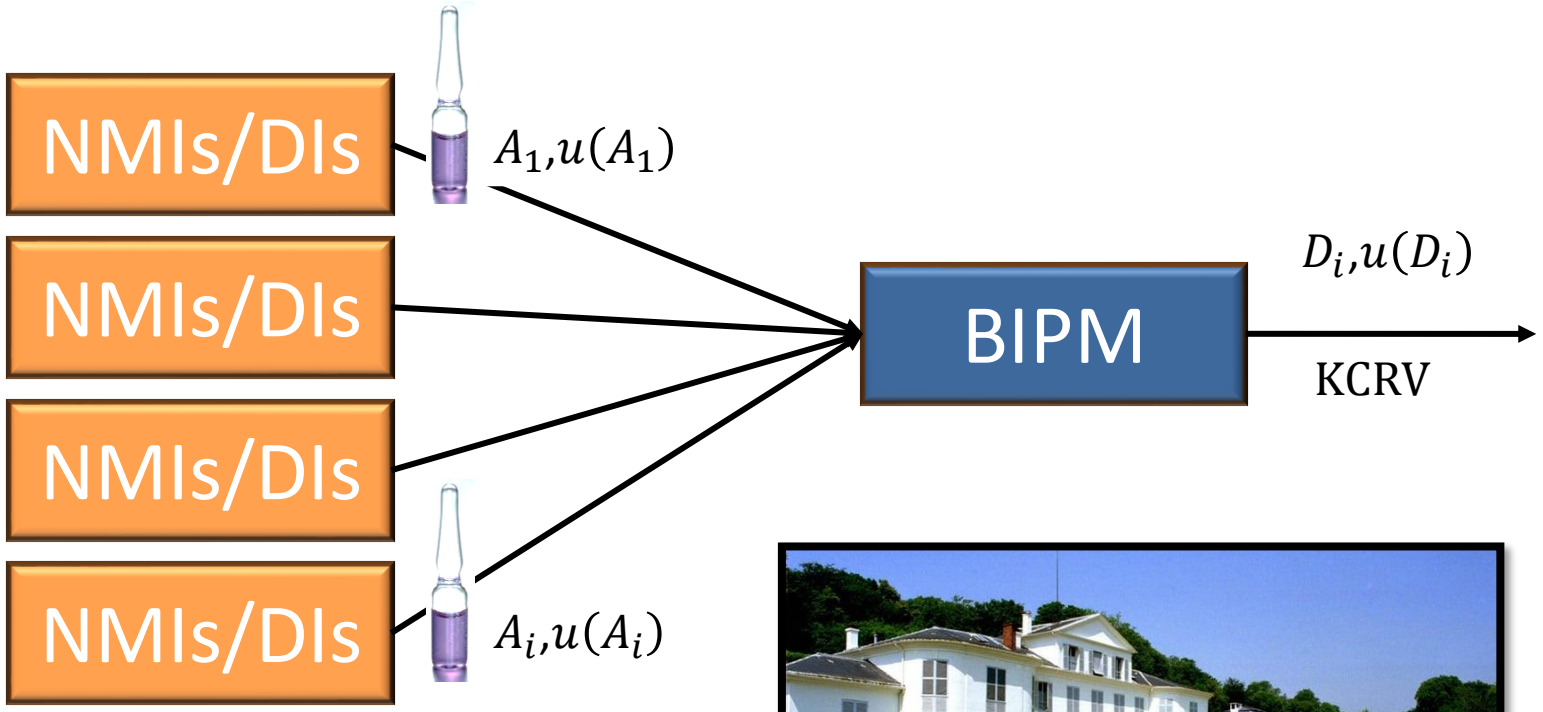
- **The Measurement Methods Matrix (MMM)**
  - allows for a single measurement comparison to support CMCs for several radionuclides using the same primary method with a similar or lower level of difficulty

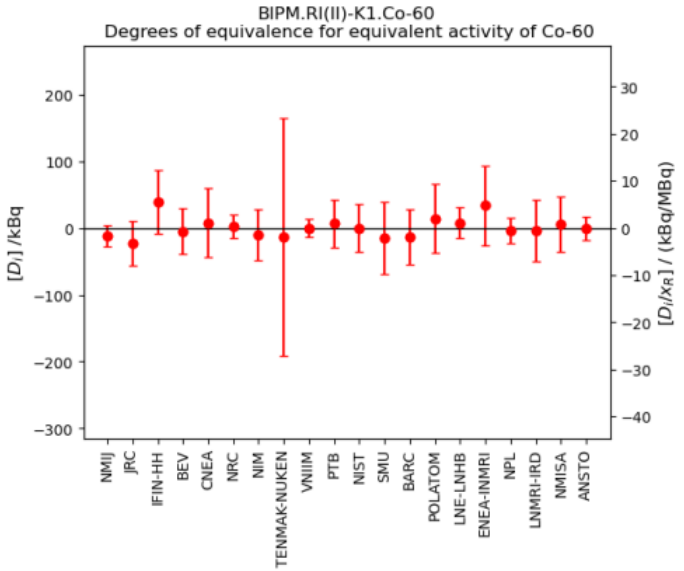


- **BIPM comparisons (SIR, SIRTI, ESIR)**
- **RMO comparisons**
  - **AFRIMETS, APMP, COOMET, EURAMET, GULFMET, SIM**
- **CCRI(II) comparisons**



BIPM “centralized and continuous” key comparisons





The BIPM runs 3 measurement services
Continuous operations

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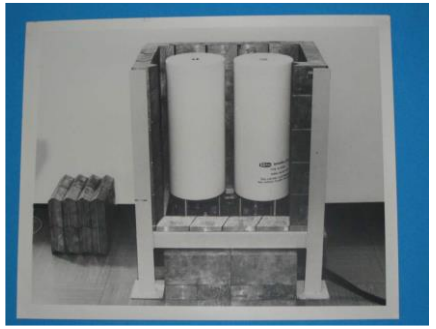
The BIPM services for radionuclide metrology

- **1976, The International System of Reference (SIR) (γ rays emitters)**
  - Ionization chambers + specific approach [Rytz, A. (1978) *Env. Int.* 1(1–2), 15]
  - 72 radionuclides et 788 independent results

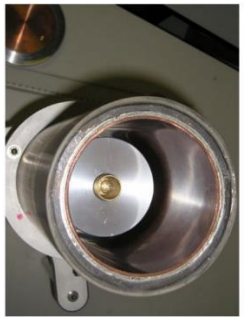
BIPM.RI(II)-K1



The SIR, since 1976

- **2009, The SIRTI (short-lived radionuclides – NMIs far from BIPM)**
  - Well type NaI(Tl) detector shipment to the laboratory
  - ^{99m}Tc (6 h), ^{18}F (2 h), ^{11}C (20 min), ^{64}Cu (13 h), ^{123}I (13 h), ^{153}Sm (2 j)

BIPM.RI(II)-K4



The SIRTI, since 2009

- **2024, The ESIR (the other radionuclides)**
  - Liquid scintillation counting + TDCR method
  - ^{14}C, ^{35}S, ^{45}Ca, ^{55}Fe, ^{63}Ni, ^{89}Sr, ^{90}Sr, ^{147}Pm, ^{99}Tc, ^{241}Am, ^{241}Pu

BIPM.RI(II)-K5

The ESIR, in 2024

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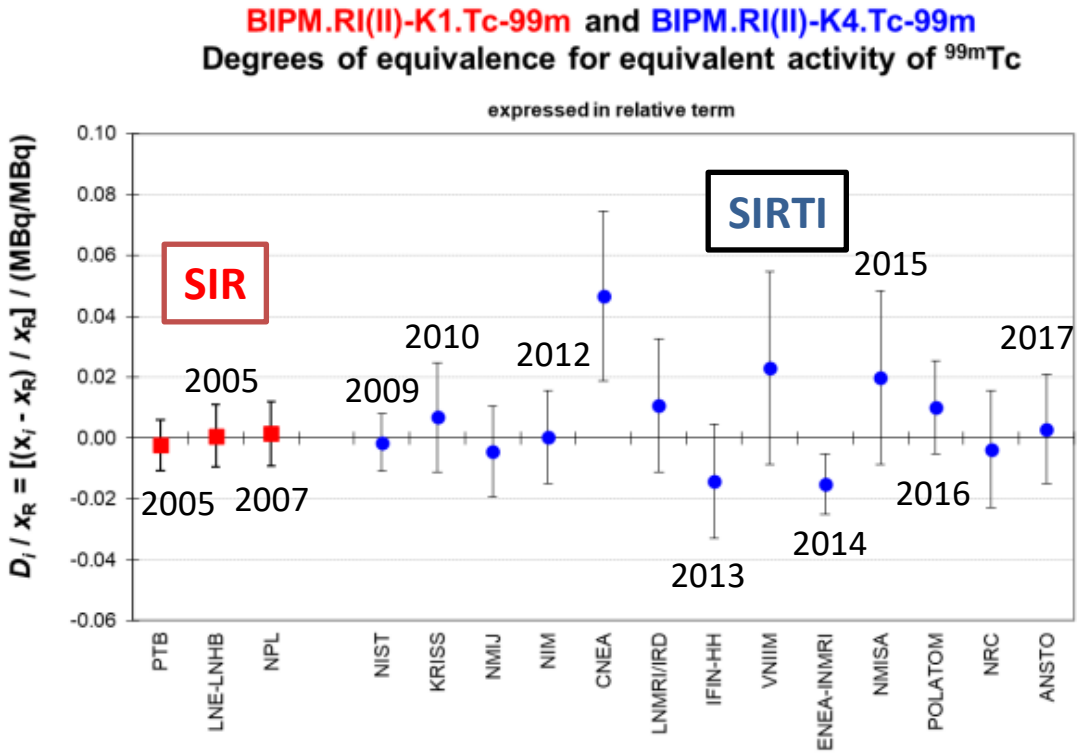
Part 2. The level of international equivalence of standards for radiopharmaceuticals

SPECT radionuclides

- Electron capture decaying radionuclides with γ rays in the range 100 keV - 300 keV
  - *Primary standardization: x-ray or Auger coincidence/ anticoincidence*
  - *BIPM services: SIR and SIRTI*
- *On market drugs*
  - **^{99m}Tc (from ^{99}Mo, $T_{1/2}$ < 1 d):**
    - **34 CMCs, 13 DoEs, KCs (1 coming, 5 planned)**
  - **^{201}Tl (cardiac scintigraphy):**
    - **18 CMCs, 4 DoEs**
  - **^{67}Ga:**
    - **26 CMCs, 3 DoEs, KCs (1 coming, 1 planned)**
  - **^{111}In (brain):**
    - **20 CMCs, 2 DoEs**
  - **^{123}I (nervous sys, thyroid, $T_{1/2}$ < 1 d):**
    - **15 CMCs, 0 DoEs (deprecated), KCs (4 coming, 2 planned)**



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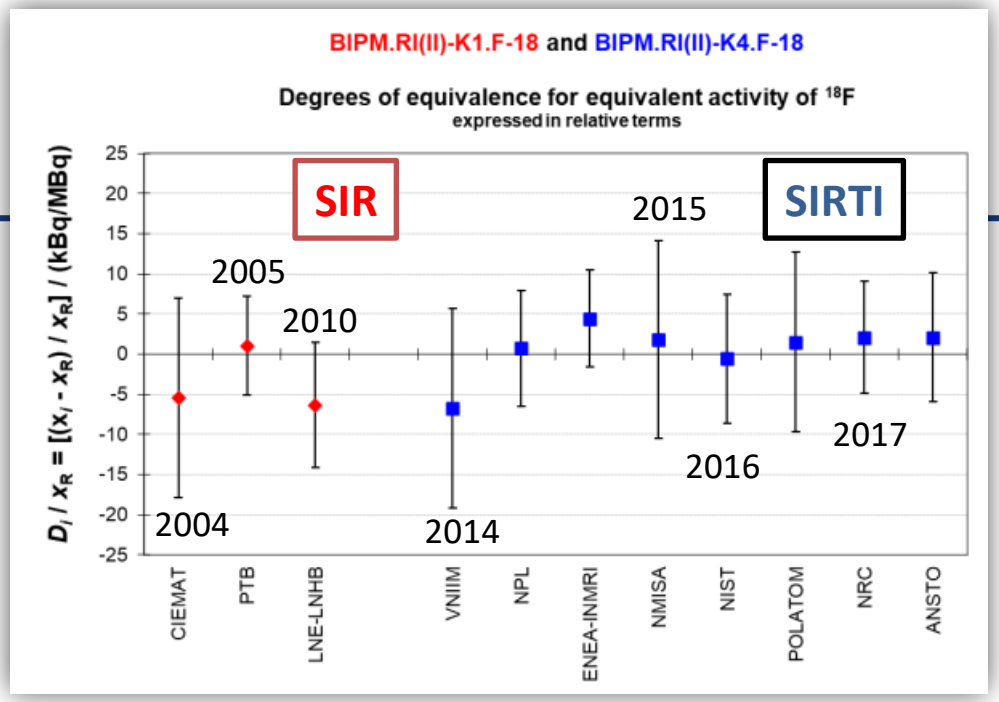
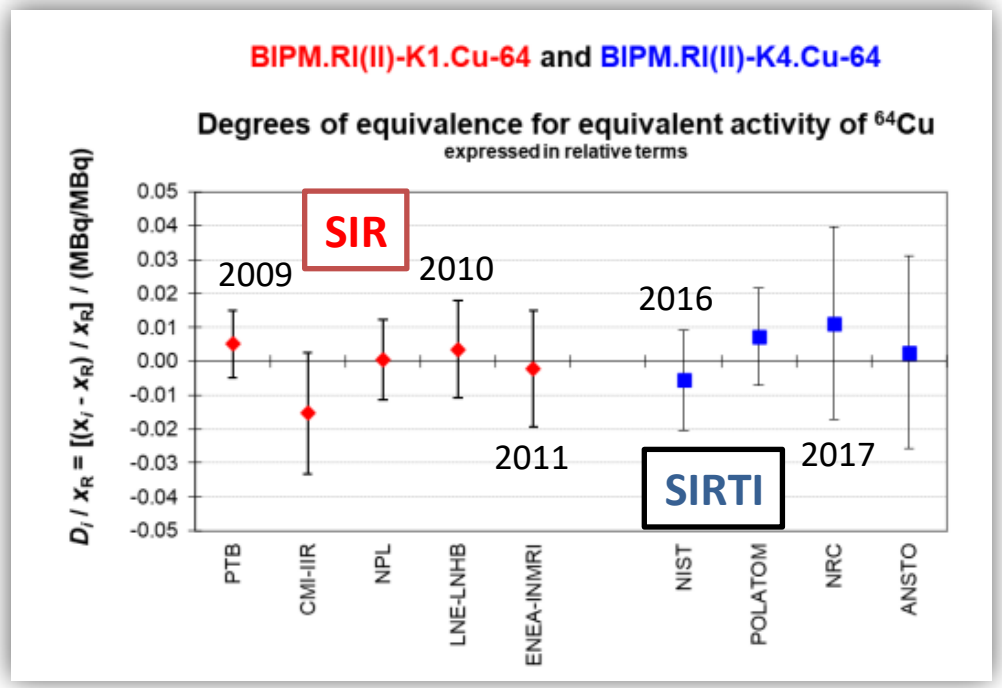
PET radionuclides

- β⁺ decaying radionuclides ($T_{1/2} < 1$ d)
  - Primary standardization: β-γ coincidence/ anticoincidence
  - *BIPM services: SIR and SIRTI*
- On market:
  - **^{18}F: 19 CMCs, 12 DoEs, KCs (3 coming, 6 planned)**
  - **^{64}Cu (neuroendocrine tumors, ^{67}Cu pairs):**
    - **6 CMCs, 9 DoEs, KCs (2 coming, 3 planned)**
  - **^{11}C (prostate): 4 CMCs, 1 KCs (NRC), KCs (2 planned)**
  - **^{68}Ga (neuroendocrine tumors, from ^{68}Ge): 7 CMCs, 0 DoE**
- Investigate:
  - **^{124}I: 2 CMCs, 0 DoE**
  - **^{152}Tb (in theranostic pairs with ^{161}Tb or ^{149}Tb): 0 CMCs, 0 DoEs**
  - **^{44}Sc (in theranostic pairs with ^{47}Sc): 0 CMCs, 0 DoEs**
  - **^{52}Mn: 2 CMCs, 0 DoEs**





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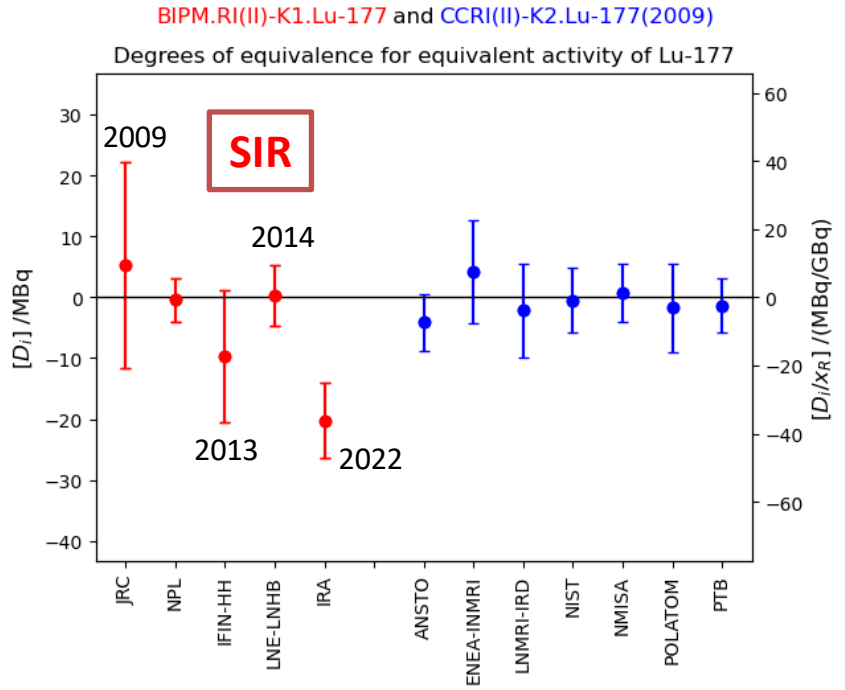
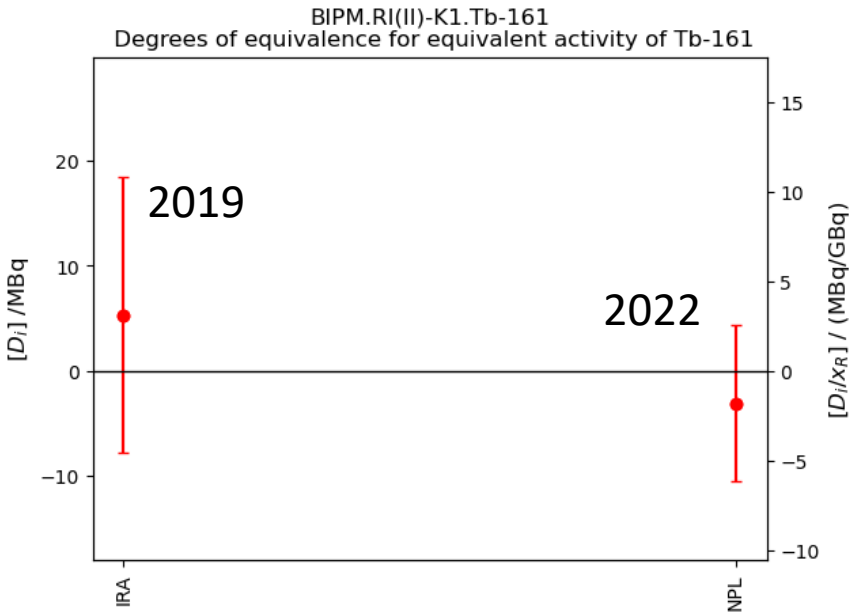
Theranostics: β therapy + SPECT

- β⁻ decaying radionuclides
  - *Primary standardization: β-γ coincidence/ anticoincidence*
  - *BIPM services: SIR and SIRTI*
- On market
  - **^{131}I (thyroid): 48 CMCs, 18 DoEs**
  - **^{177}Lu (neuroendocrine tumors): 8 CMCs, 12 DoEs, KCs (2 coming, 1 planned)**
  - **^{153}Sm (bone cancer, $T_{1/2}$ < 2 d): 13 CMCs, 0 DoEs (deprecated), KCs:**
    - **2 coming with the SIR (PTB, CMI)**
    - **1 coming with the SIRTI + 3 planned with the SIRTI**
- Investigate:
  - **^{161}Tb (in pair with ^{152}Tb): 0 CMCs, 2 DoEs, CCRI(II) K2 planned**
  - **^{111}Ag: 0 CMCs, 0 DoE, KCs (1 coming)**
  - **^{47}Sc (pair with ^{44}Sc): 2 CMCs, KC results deprecated**
  - **^{67}Cu (pair with ^{64}Cu): 0 CMCs, 0 DoEs**
  - **^{166}Ho (bone cancer): 1 CMC, 1 KC result, KCs (2 planned)**





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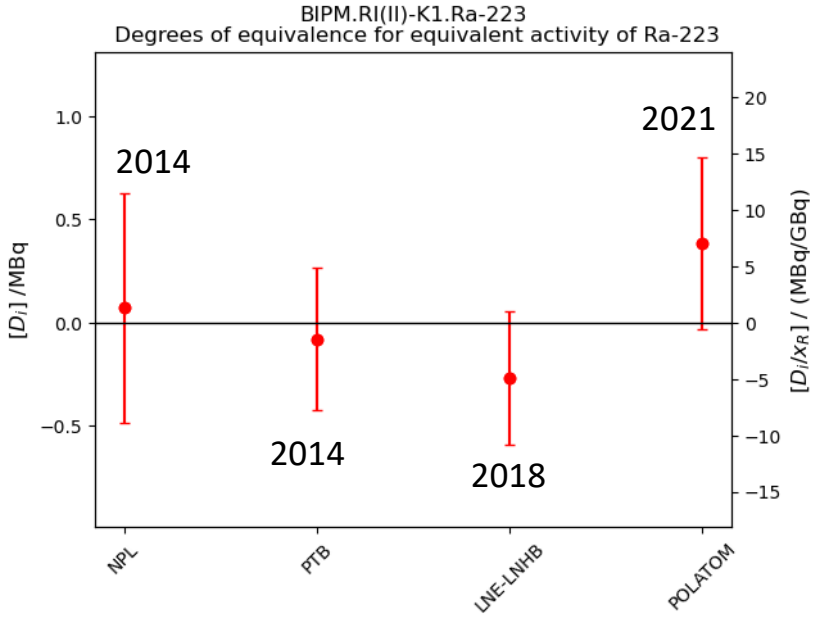
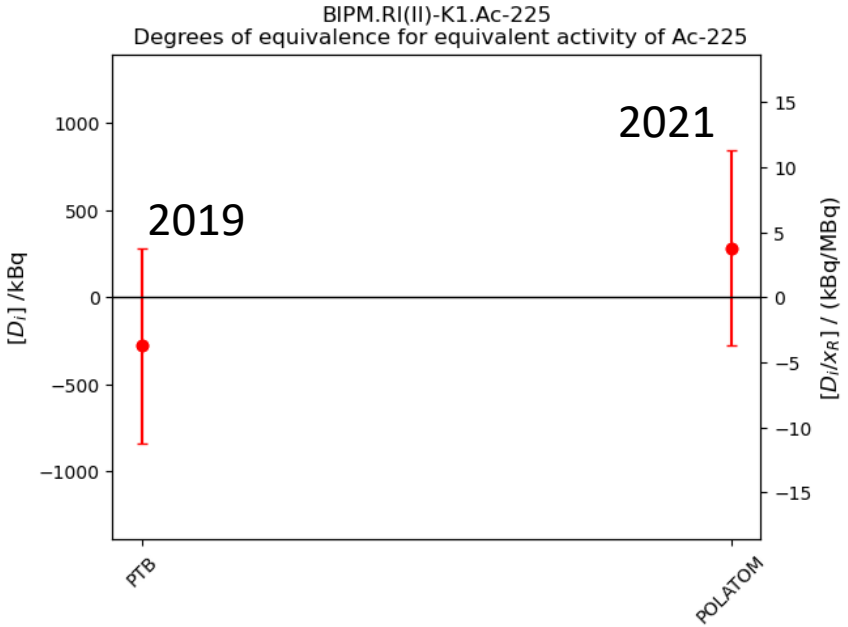
Theranostics: α therapy + SPECT or PET

- α decaying radionuclides
  - *Primary standardization: Liquid scintillation counting, C/N, TDCR, 4π(LS)α-γ*
  - *BIPM services: SIR and SIRTI, (ESIR)*
- On market
  - **^{223}Ra (bone metastasis): 0 CMCs, 4 DoEs, KC (1 planned)**
- Investigate
  - **^{225}Ac (Myeloid Malignancies): 0 CMCs, 2 DoEs, KCs (1 coming + 1 planned + CCRI(II) K2 planned)**
  - **^{227}Th: 0 CMCs, KC (1 planned)**
    - **Standardization of ^{227}Th: Collins, S. (2019) ARI 145 240-250**
  - **^{211}At: 0 CMCs, 0 DoE**
  - **^{212}Bi (in ^{212}Pb chain): 0 CMCs, 0 DoE**
  - **^{213}Bi (in ^{225}Ac chain): 0 CMCs, 0 DoE**
  - **^{149}Tb (PET, pair with ^{152}Tb): 0 CMCs, 0 DoE**





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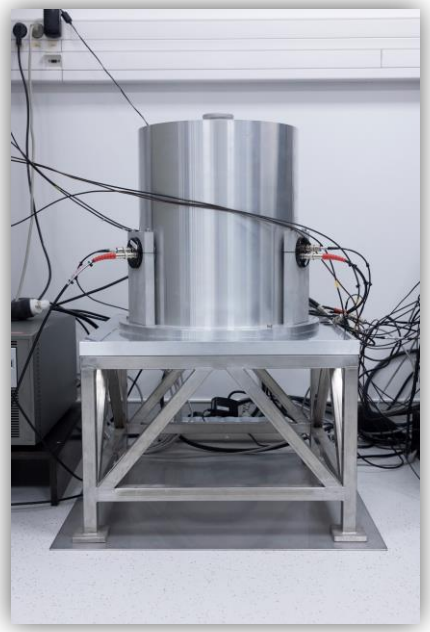
Auger and β therapy

- Ec or β decaying radionuclides
  - *Primary standardization: Liquid scintillation counting, C/N, TDCR*
  - *BIPM services: ESIR*
- On market
  - **^{90}Y (from ^{90}Sr, hepatic cancer): 66 CMCs, 0 DoE, (ESIR open)**
  - **^{89}Sr (bone cancer): 80 CMCs, 0 DoE, (ESIR open)**
- Investigate
  - **^{32}P: 34 CMCs, 0 DoE, (ESIR open)**
  - **^{169}Er: 0 CMCs, 0 DoE**
    - **Standardization of ^{169}Er: Talip, Z. (2021) ARI 176 109823**
  - **^{135}La ($T_{1/2}$ < 2 d): 0 CMCs, 0 DoE**
  - **^{165}Er (from ^{165}Tm, $T_{1/2}$ < 2 d): 0 CMCs, 0 DoE**



BIPM.RI(II)-K5 comparison opened for ^{89}Sr, ^{90}Y, ^{32}P

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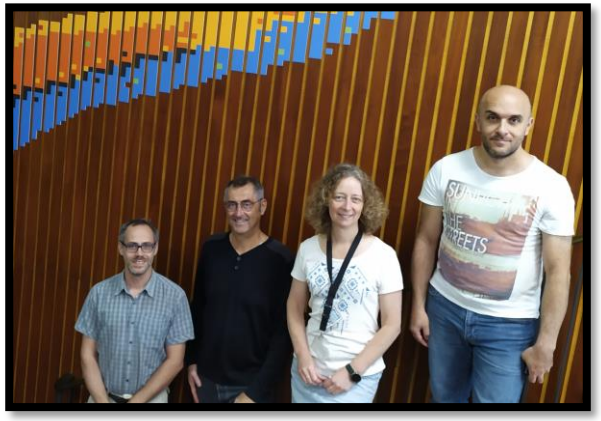
Conclusion

- The traceability of nuclides of interest to medicine is well supported by Key Comparisons
- Notably through the support of BIPM measurement services,
  - The SIR and the SIRTI provide an active support to
    - The on-market SPECT nuclides: ^{99m}Tc, ^{201}Tl, ^{67}Ga, ^{111}In
    - The on-market PET nuclides: ^{18}F, ^{64}Cu
    - **The SIRTI will soon produce equivalence for ^{123}I (SPECT) and ^{11}C (PET)**
  - The SIR provides an active support to theragnostic nuclides:
    - β therapy + SPECT: ^{131}I, ^{177}Lu, ^{161}Tb
    - α therapy + SPECT: ^{223}Ra, ^{225}Ac
    - **The SIR/SIRTI will soon produce equivalence for ^{153}Sm (β therapy + SPECT)**
  - **The new ESIR is ready to evaluate equivalence of β therapy nuclides: ^{89}Sr, ^{90}Y and ^{32}P**

Thank you for your attention.

17:30 – Laboratory tour



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SPECT only radionuclides

Rad.	Decay	$T_{1/2}$	BIPM Service	CMCs	
^{99m}Tc	I.T. / γ (141 keV)	6 h	SIR **** SIRTI **********	34	From ^{99}Mo
^{67}Ga	ε / γ (93, 185 et 300 keV)	3.3 d	SIR ********** c	26	
^{169}Yb	ε / γ (63 et 198 keV)	32 d	SIR **********	24	
^{111}In	ε / γ (171 et 245 keV)	2.8 d	SIR **********	20	
^{201}Tl	ε / γ (167 keV)	3.0 d	SIR **********	18	
^{123}I	ε / γ (159 keV)	13.2 h	SIR ****** c SIRTI *****	15	
^{155}Tb	ε / γ (45, 87, 105 keV)	5.3 d	-	0	Part of the Tb theranostic quadruplet

« * » outdated
« * » valid
« * » on going
« * » planned

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PET only radionuclides

Rad.	Decay	$T_{1/2}$	BIPM Service	CMCs	
^{18}F	β^+/γ (511keV)	1.8 h	SIR ***** SIRTI **********	19	
^{64}Cu	$\beta^+,\beta^-/\gamma$ (511keV)	12.7 h	SIR ****** SIRTI *********	6	
^{11}C	β^+/γ (511keV)	20.3 min	SIRTI ***	4	
^{124}I	β^+/γ (511 – 603 keV)	4.2 d	SIRTI **	2	
^{68}Ga	β^+/γ (511 keV)	68 min	-	7	From ^{68}Ge
^{52}Mn	β^+/γ (511 keV)	5.6 d	-	2	
^{152}Tb	β^+/γ (511 – 344 keV)	17.5 h	-	0	In theranostic pairs with ^{161}Tb or ^{149}Tb
^{44}Sc	β^+/γ (511 – 1157 keV)	4.0 h	-	0	In theranostic pairs with ^{47}Sc

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β therapy + SPECT

Rad.	Decay	$T_{1/2}$	BIPM Service	CMCs	
^{131}I	β^-/γ (364 keV)	8.0 d	SIR ********** ********** **********	48	environment
^{153}Sm	β^-/γ (103 keV)	1.9 d	SIR **** ** c SIRTI * ***	13	
^{177}Lu	β^-/γ (208 keV)	6.6 d	SIR ** ********** ** * c	8	
^{47}Sc	β^-/γ (160 keV)	3.4 d	SIR ***	2	In pairs with ^{44}Sc (PET)
^{161}Tb	β^-/γ (48, 75 keV)	6.9 d	SIR ** c	0	In pairs with ^{152}Tb (PET)
^{166}Ho	β^-/γ (1379 keV)	26.8 h	SIR * c	1	
^{111}Ag	β^-/γ (342 keV)	7.5 d	SIR * c	0	
^{67}Cu	β^-/γ (184 keV)	2.6 d	-	0	In pairs with ^{64}Cu (PET)
^{199}Au	β^-/γ (158 keV)	3.1 d	-	0	
^{175}Yb	β^-/γ (396, 283 keV)	4.2 d	-	0	

« * » outdated
« * » valid
« * » on going
« * » planned

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α therapy + SPECT or PET

« * » outdated
« * » valid
« * » on going
« * » planned

α therapy + SPECT

Rad.		Decay	$T_{1/2}$	BIPM Service	CMCs	
^{223}Ra	**α therapy + SPECT**	**α (MeV) / γ (81-98, 269, 351 keV)**	**11.4 d**	**SIR **** * c**	**0**	**^{219}Rn, ^{215}Po, ^{211}Pb, ^{211}Bi, ^{207}Tl**
^{225}Ac	**α therapy + SPECT**	**α (6,88 MeV) / γ (100, 218, 441 keV)**	**9.9 d**	**SIR ** * * c**	**0**	**^{221}Fr, ^{217}At, ^{213}Bi, ^{213}Po, ^{209}Pb**
^{227}Th	**α therapy + SPECT**	**α (MeV) / γ (81-98, 236, 269, 351 keV)**	**18.7 d**	*** c**	**0**	**^{223}Ra, ^{219}Rn, ^{215}Po, ^{211}Pb, ^{211}Bi, ^{207}Tl**
^{211}At	α therapy + SPECT	α (6.8 MeV) / X (78 keV)	7.2 h	-	0	
^{213}Bi	α therapy + SPECT	α (8.2 MeV) / γ (441 keV)	0.76 h	-	0	213Po -> 209Pb (3.2 h)

α therapy + PET

Rad.		Decay	$T_{1/2}$	BIPM Service	CMCs	
^{149}Tb	α therapy + PET	α (3.9 MeV) β^+/ γ (165, 352, 551 keV)	4.8 h	-	0	In pairs with ^{152}Tb (PET)

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- **Standardization of ^{227}Th: Collins, S. (2019) ARI 145 240-250**

β therapy

Applied Radiation and Isotopes 176 (2021) 109823

Rad.	Decay	$T_{1/2}$	BIPM Service	CMCs	
^{89}Sr	β^- (1495 keV)	51 d	CCRI(II) **********	80	
^{90}Y	β^- (2279 keV)	2.7 d	-	66	From ^{90}Sr, environment
^{32}P	β^- (1711 keV)	14.3 d	-	34	environement
^{169}Er	β^-(353 keV)	9.4 d	-	1	In pairs with ^{165}Er

Auger therapy + SPECT

Rad.	Decay	$T_{1/2}$	BIPM Service	CMCs	
^{135}La	ε / x (37 keV) e_A (5 keV)	18.9 h	-	0	
^{165}Er	ε / x (47 keV)	10.4 h	-	0	From ^{165}Tm

« * » outdated
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BIPM services:

- **The SIRTI, the ESIR, the ESIRTI**