# INSTITUTUL NATIONAL DE C&D PENTRU FIZICA SI INGINERIE NUCLEARA"HORIA HULUBEI"
## IFIN-HH Bucuresti ROMANIA

## The Support Offered by the Romanian Primary Activity Standard Laboratory to the Nuclear Medicine Field

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### 1. Introduction

The quality of a nuclear medicine procedure depends on the activity and quality of the radiopharmaceutical administrated, ***IAEA-TRS 454 (2006).* Contributors : Dondi, M., Herbst,… Sahagia, M.,.. Woods, M.J. , Zimmerman, B.E. *Quality Assurance for Radioactivity Measurement in Nuclear Medicine. pp.1-96. ISSN 0074-1914 no.454***, involving high precision measurement of activity (Becquerel), supported by the Primary Activity Standard Laboratories, like the RML from IFIN-HH. **Sahagia, M. (2011) Chapter 6: "*Role of the Radionuclide Metrology in Nuclear Medicine*"of the book: *„12 chapters on nuclear medicine",* Ed. INTECH, ISBN 978-953-307-802-1**

**The paper presents RML's actions and results**.

(i) **Development of installations and methods for the primary/absolute standardization** of radionuclides, internationally validated, through key or supplementary BIPM comparisons. RML's results are part of *the Key Comparison Data Base (KCDB) Annex B of the CIPM – MRA and* supplementary comparisons. Implementation of the QMS, within the standard EN ISO/IEC 17025:2005, recognized by the EURAMET TC-Q; CMC files' publication in the Annex C of the CIPM-MRA.

(ii) **Establishment of a secondary standard**, ionization chamber. The determined calibration factors allow the measurement and certification of the radiopharmaceuticals.

(iii) **Direct support to the nuclear medicine units**: delivery of radioactive standards; calibration of the Radionuclide Calibrators; organization of comparisons (ILCs) and proficiency tests (PTs).

**Calibration services for radionuclide calibrators - a 6-years work period**: check of the uncertainty; recalibration and establishment of new calibration factors (dial settings); follow up of the calibrator's behavior; comparison of the measured activity with the reference value; results of calibration check versus the participation at Proficiency Tests (PTs) organized by the RML.

### 2. Radioactive standards for nuclear medicine realized in the RML and their validation through international comparisons.

**Three types of installations were set up**: (i) a coincidence installation and method, 4πβ(PC)-γ system; (ii) a detection block for x - x,γ coincidences; (iii) a liquid scintillation counter (LSC-TDCR). They cover the necessity for absolute standardization of all medical radionuclides used in Romania.

$^{99m}$**Tc** decays by an isomer transition. It was standardized by an original coincidence method. **Sahagia, M. (2006).*Standardization of $^{99m}$Tc*. Appl. Radiat. Isot. 64, 1234-1237**. The international validation - supplementary comparison *IAEA "CCRI(II)-S6.Co-57.* 2 CMC files transmitted to the EURAMET.$^{131}$**I** decays by β-γ ray emission and was standardized by the 4πβ(PC)-γ coincidence. Validation by: *"BIPM(RII)-K1.I-131",* in *Key Comparison Data Base*: *http://kcdb.bipm.org/AppendixB/KCDB_ApB_search.asp*, and *"CCRI(II)-S6.I-131*"; two files in *Annex C - Calibration and Measurement Capabilities of the CIPM-MRA*.$^{18}$**F** was not yet standardized, but $^{64}$**Cu** and $^{68}$**Ga** : **Bé, M.-M et al.(2012). *Standardization, decay data measurements and evaluation of $^{64}$Cu.* Accept. Appl. Radiat. Isot. Sahagia, M., A. Luca, A., Antohe, A., Ivan, C. (2012). *Standardization of $^{64}$Cu and $^{68}$Ga by the 4π(PC)β-γ coincidence method and calibration of the ionization chamber.* Accepted, Appl. Radiat. Isot.** No international comparison. $^{32}$**P,** $^{89}$**Sr,** $^{90}$**Y** are pure beta, high energy emitters. For $^{32}$**P** and $^{89}$**Sr**, the LSC-TDCR method and system were applied within "CCRI(II)-K2.P-32 " and "*CCRI(II)-K2.Sr-89*" comparisons. In stead of $^{90}$**Y,** we measured the $^{90}$**(Sr+Y)** decay chain by the LSC-TDCR . $^{153}$**Sm,** $^{177}$**Lu,** $^{186}$**Re** and $^{188}$**Re** are β-γ ray emitters, and were standardized by the 4πβ(PC)-γ coincidence. For $^{177}$**Lu**, we participated at the "*CCRI(II)-K2.Lu-177*" comparison.$^{125}$**I** decays by electron capture process, with the emission of Auger and conversion electrons, x- and γ- rays. It was standardized by the sum-peak method or the x-x, γ coincidence; we participated at the "*CCRI(II)-K.2.I-125.*

### 3. Establishment of the secondary standard, reentrant ionization chamber CENTRONIC IG12/20A

The ionization chamber is a very stable instrument. It was calibrated for many gamma-ray radionuclides, including $^{64}$**Cu** and $^{68}$Ga. The calibration was done for : ampoules with 2 mL (PTB-Germany), 3.6 mL (SIR) and 5 mL vials (P6, penicillin), of standard solution. The validation was done via the comparisons conducted through the CIPM-MRA comparison route, Appendix B of the BIPM KCDB database and the comparison of results with the calibration by the Physikalisch Technische Bundesanstalt (PTB), Braunschweig, Germany, for 18 radionuclides, using PTB standard solutions in 2 mL vials. **Sahagia, M., Wätjen, A.C., Luca, A., Ivan, C. (2010) *IFIN-HH ionization chamber calibration and its validation; electrometric system improvement.* Appl.Radiat.Isot. 68, 1266 – 1269**

### 4. Support of RML to the nuclear medicine: delivery of radioactive standards and metrology services

The RML prepares all kinds of radioactive standards for medicine. **The most important operation is the calibration of the Radionuclide Calibrators** ; the legal metrological check was mandatory only until 2010.Several rounds of national comparisons on $^{131}$I, $^{57}$Co and $^{99m}$Tc were organized. The last ones,$^{131}$I and $^{99m}$Tc, were organized within the frame of the IAEA – CRP E2.10.05:*"Harmonization of quality practices for nuclear medicine radioactivity measurements"* **Olsovcova, V., Iwahara, A.,…Sahagia, M., …Zimmerman, B. (2010) *National Comparisons of I-131 measurement among nuclear medicine clinics of eight countries*. Appl.Radiat.Isot.68, 1371 – 1377.** The data were expressed as ratios:

$R = A_{mess} / A_{ca;}$ $A_{mess}$ is the activity measured and reported by the participants and $A_{ca}$ is the conventionally true activity, with uncertainties of 1.5 % for $^{131}$I and 3.0 % for $^{99m}$Tc, $k$ = 2 (95 % confidence level). In the case of $^{131}$I, 0.851 ≤ $R$ ≤ 1.383, with 80 % of the 12 results being compliant with the Pharmacopoeia requirement. For $^{99m}$Tc, 0.954 ≤ $R$ ≤ 1.077, with 100% of the results being compliant. The calibration of the radionuclide calibrators proved to be necessary, in order to assure the correct calibration of the instruments and to establish if the wrong results in comparisons are due to the calibrators or to the human errors in measurement. The calibrations were performed under the national RENAR accreditation , and CNCAN notification, according to the EN ISO/IEC 17025:2005

### 4.1 Calibration operations to be performed.

(i) Measurement of the background indication and decontamination, if necessary;
(ii) Preparation and measurement of standards: solution, or gelatin $^{131}$I capsules;
(iii) Calibration - Measurement of the standards with the radionuclide calibrator. Two situations can occur:
-(a) The difference from reference activity is higher than ± 10 % and the calibration factor (dial setting) is modified, or the correction factor for result is written in the certificate.
-(b) The obtained value differs from reference by less than ± 10 %; both values are written in the calibration certificate.
-The ratio ***R* is calculated as $R = A_{mess} / A_{ca}$** where $A_{mess}$ is the activity measured with the apparatus to be calibrated. Uncertainty calculation - combination of standards' ones and the values for instruments - 5 %.
(iv) Follow up of the decay of the standard , to verify the linearity of response
(v) Follow up an apparatus behavior for several years of utilization.
(vi) Check of $^{99}$Mo breakthrough in $^{99m}$Tc.

### 4.2 Results obtained in calibration.

(a) The dial setting modification was done for two old calibrators Picker . For old Curiementor 2 and 3 calibrators, a corrective factor $f$ = (1.15 ± 0.03) was recommended.
(b) The mean values for cases with differences less than ± 10 % are presented in Table 1, for the main types of calibrators.

**Table 1: Calibration results**

| Mean ratios $R = A_{mess} / A_{ca}$ | Type of calibrator | $R$, $^{99m}$Tc | $R$, $^{131}$I |
|---|---|---|---|
| Mean | Curiementor 3 and ¾ | 0.964 ± 0.022 | 0.973 ± 0.008 |
| Mean | CRC-15 R and 25 R | 1.031 ± 0.001 | 1.008 ± 0.012 |
| Mean | Picker and Picker MicroCal | 0.993 ± 0.006 | 1.009 ± 0.034 |
| Mean | All calibrators | 0.978 ± 0.032 | 0.995 ± 0.023 |

**Discussion of Table 1 results**

**All the calibrators, except two Curiementor 3 units, $^{99m}$Tc, differ by less than (- 5 %) from the conventionally true (reference) activity.**

**$^{99m}$Tc calibration: The Curiementor calibration is (- 3.6 %) different from the reference, while the Capintec calibration is (+ 3.1 %), what means that the measurements of the same recipient with solution with the two types of instruments differ by 6.6 %; the Picker calibration is different by (- 0.7 %).**

**$^{131}$I, calibration: the calibrations are (- 2.7 %) for Curiementor and (+ 0.8 %) for Capintec; the Picker difference is (+ 0.9 %).**

**The mean ratio of all Calibrators is in agreement with the reference value**

**Table 2: Linearity test, $^{99m}$Tc decay during a 24 h interval**

| Activity, MBq | 1400 | 1225 | 972 | 97 | 76 |
|---|---|---|---|---|---|
| *R*atio between the measured and calculated activity Curiementor 3 | 1.0000 | 0.9974 | 1.0036 | 1.0014 | 1.0010 |
| *R*atio between the measured and calculated activity Capintec CRC 15R | 1.0000 | 1.0008 | 1.0002 | 0.9968 | 1.0041 |

**The linearity is satisfactory enough, for activities from 70 MBq up to 1400 MBq,**
**The differences from the calculated and measured activities is in all cases less than 0.5 %.**

**Table 3: Long term behavior, $^{131}$I measurement**

| Year / *R* | 2006 | 2009 | 2010 | 2011 |
|---|---|---|---|---|
| Capintec CRC-15 R/1 | 0.999 ± 0.051 solution | 1.004 ± 0.051 capsules | 1.003 ± 0.051 solution<br>1.020 ± 0.051 capsules | 1.003 ± 0.051 solution<br>1.020 ± 0.051 capsules |
| Capintec CRC-15 R/2 | 1.005 ± 0.051 solution | 0.989 ± 0.051 capsules | 1.009 ± 0.051 solution | 1.009 ± 0.051 solution |

**In the case of solution, the stability is better than 0.9 %, with no trend in indication variation, while for capsules measurement it can reach maximum 2 %.**

**$^{99}$Mo breakthrough ($^{99m}$Tc purity). Only a few calibrators are provided with the lead shield : the $^{99}$M content in the solution was less than 0.001 from $^{99m}$Tc activity**

### 5. Conclusions

**- The paper presents the support given by the RML, IFIN-HH, to the Romanian units involved in nuclear medicine, for assuring the whole metrological traceability chain, from the SI up to the end users, nuclear medicine units.**
**- The most relevant direct support consists in the calibration of radionuclide calibrators.**
**- Every year the operation was amplified in volume.**
**- New, high quality, instruments were purchased by the nuclear medicine units.**
**- The majority of calibrators' indication differs by < ± 5 % from the reference; the erroneous results obtained in comparisons are mainly due to the human errors in measurement.**

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