METROLOGICAL TRACEABILITY ASSURANCE IN PRODUCTION AND USE OF RADIOPHARMACEUTICALS FOR PET IMAGING AND TARGETED RADIOTHERAPY *

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The paper presents the implication of the Radionuclide Metrology Laboratory (RML) from IFIN-HH in solving the problems connected with the quality assurance of radiopharmaceuticals in production and use, by assuring the metrological traceability in the control of the radiometrological parameters: measurement of activity and radioactive concentration, radionuclide purity as well as measurement of the decay scheme parameters. The following problems are treated: (i) Absolute standardization of PET radionuclides: $^{64}$Cu and $^{68}$Ga and study of their decay scheme parameters; absolute standardization of radionuclides used in targeted - molecular radiotherapy (MRT): $^{153}$Sm, $^{177}$Lu, $^{186,188}$Re and $^{89}$Sr, calibration of the secondary standard ionization chamber and of some commercial radionuclide calibrators. (ii) Radionuclide purity analysis and its influence on the activity calculation. The aspects presented are an overview of published papers.

Key words: radionuclide metrology, absolute standardization, positron emitters, strong beta-weak gamma emitters

1. INTRODUCTION

The modern trends in the development of nuclear medicine, based on the most effective and safe diagnostic and targeted therapy technologies, imposed the introduction in use of new types of radionuclides, with adequate physico-nuclear, chemical and biological characteristics. A new category of radionuclides, or pairs of them, “theranostic” agents, are used for both aims. They have sometimes complex decay schemes, not very well known, what raises to the radionuclide metrology community two major challenges:

– Development of absolute methods for standardization, in order to build a consistent International System of Units (SI), followed by the continuation of national chains of metrological traceability in the measurement of activity of...
radiopharmaceuticals (RPM) and elaboration of specific methods for determination of the radionuclide purity [1].

– Study of their decay scheme, regarding their half life, types of emitted radiations, their energies and emission intensities.

The need for a precise determination of the activity of a RPM, to be administrated is crucial, as its value is the determining factor in the calculation of the absorbed dose and of committed effective dose to the patient and to the medical staff [2]. In radiopharmacy and nuclear medicine units, the activity is usually determined using Radionuclide Activity Calibrators (Dose Calibrators). The manufacturers perform the calibration of the equipment in terms of calibration factors, introduced in dial settings, using sets of standard solutions, provided by the radionuclide metrology laboratories or by commercial producers, traceable to a primary standard. During the period 2004–2009, the IAEA deployed the Coordinated Research Program (CRP) E2.10.05, entitled: Harmonization of quality practices for nuclear medicine radioactivity measurements having as finality: (i) The elaboration of the document TRS454: Quality Assurance for Radioactivity Measurement in Nuclear Medicine [3]. (ii) The elaboration of protocols to be used by the network of Secondary Standard Dosimetry (Radioactivity) Laboratories [SSD(R)L] in organizing national campaigns of proficiency testing in measurement of RPMs in hospitals [4], as well as for their participation in international comparisons; two such exercises were organized within the CRP [5,6].

Within the period 2012 – 2015, the EURAMET – European Organization of National Metrology Institutes (NMIs), deploys the Joint Research Project (JRP) HLT11, MetroMRT – Metrology for Molecular Radiotherapy, http://www.euramet.org/index.php?id=emrp_call-2011#C10258, 14 participants, National Metrology Institutes and clinics, having as topic:

(i) Measurement of administrated activity; (ii) Measurement of activity within a tissue volume using quantitative imaging (QI) method (SPECT or PET);
(iii) Integration of a time-sequence of QI activity measurements to give the activity-time integral within the defined volume; (iv) Calculation of absorbed dose from the activity-time integral.

The decay scheme parameters are also directly influencing the dose, as they are input data for all used programs for its calculation. The problem has two features; the experimental determination of the values and the critical analysis and mathematical combination of them, in order to establish International Bases of Decay Data. A national primary standard laboratory, recognized at the international level, can solve entirely these tasks, by the following actions: it sets up the installations for absolute standardization of radionuclides, demonstrates its international equivalence, assures traceability to the lower levels and participates at programs for decay data study [7]. These activities have a long tradition in the IFIN-HH, RML’s activity, starting with the SPET most used radionuclides in Romania, $^{99m}$Tc and $^{131}$I [8], and continues with the new ones introduced in production and use.
2. ABSOLUTE STANDARDIZATION OF PET RADIONUCLIDES

Our laboratory dealt in the past with the absolute standardization of radionuclides with complex decay scheme, electron capture – positron emission [9]. The introduction of PET radionuclides in diagnostic imposed their systematic study, both at the international and national levels. One interesting PET emitter is $^{64}$Cu. An EURAMET project, no. 1085, Standardization, decay data measurements and evaluation of $^{64}$Cu, having as participants LNE-LNHB – France (coordinator) and PTB – Germany, CMI – Czech Republic, NPL – UK and IFIN-HH – Romania, was deployed during the period 2007–2010. The results were presented in the paper [10]. The introduction in Romania of new PET/CT facilities, working first with imported, and then with locally produced $^{18}$FDG, raised to the RML the problem of construction of a national traceability chain for it and for other positron emitters. A national research project: “Absolute standardization and study of the decay parameters for positron emitters used in PET systems. Assurance of metrological traceability” – PN-II-ID-2011-3-0070 was accepted for financing, within the period 2011 – 2014. It has as object the study of the PET radionuclides: $^{68}$Ga (2011–2012), $^{18}$F (2012–2013), $^{124}$I (2014) and the targeted therapy nuclide $^{67}$Cu (2013–2014).

2.1. ABSOLUTE STANDARDIZATION OF RADIONUCLIDES

The most suitable method for absolute standardization is the 4πβ(PC)-γ method, using an installation composed from two detection blocks - proportional counter (PC) and scintillation detector, Nal(Tl), with the electronic chains and a coincidence selector. A set of several solid sources, prepared gravimetrically from the solution are measured; the activity and activity concentration are determined. The general coincidence equations, connecting the counting rates, activity, decay scheme parameters and detection efficiencies, are [11]:

\[
N_\beta = N_0 \sum_{r=1}^{n} a_r e^{\beta_r} + (1 - e^{\beta_r}) e^{\gamma_r} \frac{e^{*}}{I}; \quad N_\gamma = N_0 \sum_{r=1}^{n} a_r e^{\gamma_r}
\]

\[
N_c = N_0 \sum_{r=1}^{n} a_r e^{\beta_r} e^{\gamma_r} + (1 - e^{\beta_r}) e^{cr} \frac{e}{I}
\]

When the variant of efficiency extrapolation is applied, the equations (1) are written in an equivalent form, where $K$ and $(1-K)$ are the extrapolation slopes:
The above mentioned positron emitters have a decay scheme of the type presented in Figure 1.

\[
N_\beta = N_0 \left( 1 - K \left( \frac{1 - N_c}{N_\gamma} \right) \right) - \frac{N_{\beta N}}{N_c} = N_0 \left( 1 + (1 - K) \left( \frac{1 - N_c}{N_\gamma N_\gamma} \right) \right)
\]

\[
K = \frac{\sum a_r C_r \left( 1 - ((\alpha \beta_{\gamma} + \beta_{\gamma}) \left( 1 + \gamma_c \right) \right)}{\sum a_r \beta_{\gamma} C_r \left( 1 - e^{\beta_{\gamma}} \right)} \frac{1 - e^{\beta_{\gamma}}}{1 - e^{\beta_{\gamma}}}
\]

The coincidence method in the variant of the efficiency extrapolation is possible in two ways: (a) the exclusive counting of the positrons/electrons in the PC and of the annihilation quanta in the gamma detector; (b) the counting of all radiations in the PC and in the gamma detector and of all the possible coincidences.

The secondary method of high resolution HPGe gamma-ray spectrometry, using a calibrated system in energy and detection efficiency, can be used both for the measurement of activity and activity concentration.

2.1.1. Standardization of $^{64}$Cu and $^{68}$Ga

The results obtained in the absolute standardization of $^{64}$Cu and $^{68}$Ga and comparison with gamma-ray spectrometry are presented in the paper [12].
Table 1
Activity concentration of $^{64}$Cu and $^{68}$Ga

<table>
<thead>
<tr>
<th>Radionuclide/Parameters</th>
<th>Coincidence measurement</th>
<th>Gamma-ray Spectrometry</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Variant (a)</td>
<td>Variant (b)</td>
</tr>
<tr>
<td>$^{64}$Cu</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$f$, impurity correction</td>
<td>1.0010</td>
<td>1.0018</td>
</tr>
<tr>
<td>($^{64}$Cu, $^{68}$Ga)</td>
<td>16540±350</td>
<td>15850±340</td>
</tr>
<tr>
<td>$^{68}$Ga</td>
<td></td>
<td></td>
</tr>
<tr>
<td>($^{68}$Ga, $^{68}$Ge)</td>
<td>27790±270</td>
<td>27560±190</td>
</tr>
</tbody>
</table>

The uncertainty budgets contain the following components: standard deviation (type A) and type B uncertainties: (i) for coincidence method – dead and resolution times, background counting rates, decay scheme parameters, impurities content, weighing, time measurements and positron annihilation positions; (ii) for gamma-ray spectrometry – system calibration uncertainty as most important component, software, decay scheme, etc. Standardization of $^{18}$F and its traceability chain are treated in the paper [13].

2.2. DETERMINATION OF RADIONUCLIDE IMPURITY LEVEL.

The most used method for the determination of gamma-ray emitting radionuclide impurity is the gamma-ray spectrometry. It has some limitations: (i) non-detection of alpha- and beta-emitting impurities, for which other methods, like liquid scintillation counting, are used. (ii) existence of other positron emitting impurities, or $^{68}$Ge breakthrough in $^{68}$Ga.

2.2.1. Radionuclide $^{64}$Cu

The impurities were determined by the gamma-ray spectrometry; a mean value was calculated for the middle of measurement interval and subtracted from the PC counting rates. The content on the reference time was: $^{57}$Co: 0.55(7) x 10$^{-4}$; $^{56}$Co: 0.076(3) x 10$^{-4}$; $^{58}$Co: 0.070(5) x 10$^{-4}$; $^{67}$Cu: 0.23(14) x 10$^{-7}$. In conditions (a) only beta-radiations contributed to the PC counting rate, and the impurity correction factor was $f=1.001$; for (b) conditions, both the (X, A) and beta radiations contributed and $f=1.0018$ (Table 1).

2.2.2. Radionuclide $^{68}$Ga

The suspected impurity is the mother radionuclide $^{68}$Ge, which decays also to $^{68}$Ga. The measurement was done after 25.5 hours from reference time, when $^{68}$Ga
decreased by a factor of $5.5 \times 10^6$ times. The sum activity of all 5 sources used for absolute standardization was re-measured by coincidence; the activity of $^{68}$Ge was the difference of the obtained value and the residual calculated $^{68}$Ga activity. The activity ratio $^{68}$Ge/$^{68}$Ga, at reference time, was evaluated as: $7.3 \times 10^{-6}$.

2.3. STUDY OF THE DECAY SCHEME PARAMETERS OF PET RADIONUCLIDES

The studied decay data parameters were: half life and emission intensities of the gamma-rays; particularly, from the intensity of annihilation quanta one calculates the branching ratio of the positron decay in a complex decay scheme. The results are presented in the papers [10, 13, 15].

2.3.1. Determination of the half life

The radionuclide metrology laboratories use ionization chambers for this kind of measurements due to their excellent stability. The half-lives of $^{64}$Cu and $^{68}$Ga were measured at IFIN-HH using the chamber CENTRONIC IG12/20A. Corrections for background and decay during the measurement period of an individual data point were applied to the experimental data. The half-life was fitted for each data set of the radionuclides using a linear least-squares method. An equation in a semi-logarithmic presentation was used:

$$\log_{10}(I) = \log_{10}(I_0) - 0.30103 \cdot \frac{t}{T_{1/2}}$$

$I_0$ is the ionization current at a given time $t$ and $I_0$ is the ionization current at reference time, $t_0$; $T_{1/2}$ is the half-life of the considered radionuclide. Table 2 presents the obtained results, as compared with those published in [10] and in Table of Radionuclides (ToR) [14], 1983 data.

<table>
<thead>
<tr>
<th>Radio nuclide</th>
<th>Measurement conditions (no. of points – duration)</th>
<th>Determined value, h</th>
<th>ToR value, h</th>
<th>Difference from ToR,%</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{64}$Cu</td>
<td>19 points – 23 h</td>
<td>12.696±0.012</td>
<td>12.703±0.013 [10]</td>
<td>−0.055</td>
</tr>
<tr>
<td>$^{68}$Ga</td>
<td>14 points – 3.25 h</td>
<td>1.131±0.0017</td>
<td>1.1285±0.0010 [14]</td>
<td>+0.24</td>
</tr>
</tbody>
</table>

2.3.2. Determination of emission intensity and branching ratios

The method is the high resolution gamma-ray spectrometry using a system based on HPGe detector, calibrated in energy and efficiency. When the activity of the measured source is not precisely known, only relative emission intensities,
reported to the highest emission radiation are determined. For the determination of the absolute values it is necessary to use sources standardized absolutely, by a method non dependent of emission intensity, as for example the coincidence method in the variant of efficiency extrapolation. This was the case with our determinations. The positron emitters pose a supplementary problem: the emission of annihilation quanta, as intensity and direction, depends strongly on the annihilation position; in this case the standard sources to be used were introduced between aluminium foils, 1.3 mm thick. The standard sources of $^{64}$Cu and $^{68}$Ga were measured at distances of: 0 mm; 4.3 mm; 98.3 mm and 317 mm from the detector surface and mean values were calculated. The relations used for calculation were:

$$I_{\gamma_1}^{rel} = \frac{N \cdot \varepsilon_R}{N_R \cdot \varepsilon} \cdot 100 \text{ (per cent)} ; I_{\gamma_1} = \frac{N}{t \cdot A \cdot \varepsilon}$$

$I_{\gamma_1}$ and $I_{\gamma_1}^{rel}$ are relative and absolute intensities of the $i$-th radiation; $t$ – measuring time(s); $A$ – activity (Bq); $\varepsilon$ and $\varepsilon_R$ are detection efficiencies of the radiations “$i$” and reference (“$R$”); $N$ and $N_R$ are net areas of the full absorption peaks. Table 3 presents the final results in terms of absolute intensities.

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Radiation Energy, keV</th>
<th>IFIN-HH, RML Determined intensity (per 100 decays) [15]</th>
<th>ToR published intensity (per 100 decays)</th>
<th>(IFIN-HH – ToR) /ToR, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{64}$Cu</td>
<td>511</td>
<td>35.3 ± 1.2</td>
<td>35.04 ± 0.30 [10]</td>
<td>+0.74</td>
</tr>
<tr>
<td></td>
<td>1345</td>
<td>0.481 ± 0.017</td>
<td>0.474 ± 0.0033</td>
<td>+1.48</td>
</tr>
<tr>
<td>$^{68}$Ga</td>
<td>511</td>
<td>181 ± 6</td>
<td>178.28 ± 0.22 [14]</td>
<td>+1.53</td>
</tr>
<tr>
<td></td>
<td>578.5</td>
<td>0.044 ± 0.010</td>
<td>0.0335±0.0017</td>
<td>+31.3</td>
</tr>
<tr>
<td></td>
<td>805.8</td>
<td>0.087 ± 0.01</td>
<td>0.094±0.003</td>
<td>-17.0</td>
</tr>
<tr>
<td></td>
<td>1077.3</td>
<td>3.25 ± 0.111</td>
<td>3.22±0.03</td>
<td>+0.93</td>
</tr>
<tr>
<td></td>
<td>1261.1</td>
<td>0.084 ± 0.009</td>
<td>0.094±0.03</td>
<td>-10.6</td>
</tr>
<tr>
<td></td>
<td>1883.2</td>
<td>0.128 ± 0.013</td>
<td>0.137±0.004</td>
<td>-6.57</td>
</tr>
</tbody>
</table>

3. ABSOLUTE STANDARDIZATION OF THE RADIONUCLIDES USED FOR MOLECULAR RADIOThERAPY

The traditional radionuclide most used in targeted therapy is $^{131}$I. The extension of the beta-gamma emitters in therapy is possible by use of strong beta - weak gamma emitters, like: $^{153}$Sm, $^{177}$Lu, $^{186}$Re, $^{188}$Re. One of the emergent radionuclides, used in conjunction with the PET radionuclide $^{64}$Cu, as a theranostic pair, is $^{67}$Cu. The weak gamma ray emissions, regarding energy and intensity, are
used for their bio distribution monitoring, while avoiding long range irradiation of the body. Our laboratory standardized the radionuclides: $^{153}$Sm, $^{177}$Lu, $^{186}$Re, $^{188}$Re and planned to standardize $^{67}$Cu. Another category are the pure beta emitter radionuclides, like $^{32}$P, $^{89}$Sr, $^{90}$Y, which are absolutely standardized by using a liquid scintillation counter (LSC), with liquid scintillator or Čerenkov measurement, or the 4n\(\beta\)PC-\(\gamma\) method in the efficiency tracer variant. In this respect, a common project, Institute of Atomic Physics (IAP), IFIN-HH, RML, Romania – Commissariat a l’Energie Atomique (CEA), LNE, LNHB, France: Creation of national standards for some emerging pharmaceutical radionuclides to ensure the radioprotection of patients and medical staffs deployed during the period: 2012–2015, proposes to study the therapeutic $^{177}$Lu, $^{186}$Re, $^{90}$Y and the PET series $^{82}$Sr\(+\)Rb.

For applying the coincidence variants, an idea [16] was to treat in a unified manner the two situations: (i) the mixture – tracer with pure beta emitter; (ii) radionuclide with significant decays to the ground level of the daughter radionuclide – triangular scheme radionuclides.

The common equations, deduced from the general formulae (1), are:

$$\frac{N_\beta}{N_0} = 1 - (1 - \frac{N}{N_\gamma}) \sum_{r=1}^{n-1} a_r \frac{(1 - \frac{ae}{\beta} + \frac{e}{\beta} \frac{r}{\gamma})}{(1 - \frac{e}{\beta} \frac{r}{\gamma})} - a_n(1 - \frac{e}{\beta} \frac{n}{\gamma})$$

Equation (5) can be written in an equivalent form:

$$\frac{N_\beta}{N_0} = 1 - L(1 - \frac{N}{N_\gamma}) - a_n (1 - \frac{e}{\beta} \frac{n}{\gamma})$$

Table 4 reproduces the published results for the radionuclides $^{153}$Sm, $^{177}$Lu, $^{186}$Re, $^{188}$Re [17-19].

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Extrapolation slope (1-L)</th>
<th>(N_0/m), kBq/g</th>
<th>Combined uncertainty, u.%, k=1</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{153}$Sm</td>
<td>0.207(6)</td>
<td>487.5</td>
<td>0.82</td>
</tr>
<tr>
<td>$^{186}$Re</td>
<td>0.279(94)</td>
<td>649.9</td>
<td>0.49</td>
</tr>
<tr>
<td>$^{188}$Re</td>
<td>0.142(10)</td>
<td>1079.1</td>
<td>0.12</td>
</tr>
<tr>
<td>$^{186}$Re + $^{188}$Re</td>
<td>0.162(32)</td>
<td>2654</td>
<td>0.45</td>
</tr>
<tr>
<td>$^{177}$Lu</td>
<td>0.300(14)</td>
<td>825.6</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>0.283(13)</td>
<td>706.92</td>
<td>0.67</td>
</tr>
</tbody>
</table>
The pure beta radionuclide, $^{89}\text{Sr}$, was standardized by both methods: The liquid scintillation counting, Triple to Double Coincidence Ratio (LSC-TDCR) and efficiency tracer method, using as tracer a $^{60}\text{Co}$ standard solution. We participated at the key comparison type K2. The results for two methods are presented in the Table 5 [20].

<table>
<thead>
<tr>
<th>Standardization method</th>
<th>Radioactive concentration, kBq g$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquid scintillation counting</td>
<td>26.09 ± 0.21</td>
</tr>
<tr>
<td>Tracer method</td>
<td>26.58 ± 0.29</td>
</tr>
</tbody>
</table>

4. INTERNATIONAL VALIDATION OF THE STANDARDIZATION METHODS FOR MOLECULAR THERAPY RADIONUCLIDES

Our laboratory has participated at international comparisons on the measurement of activity (Bq) and activity concentration (Bq g$^{-1}$) since 1962, for all kinds of radionuclides. A particular category of interest are the medical radionuclides, for which RML participated at key comparisons, within the CIPM-MRA (International Committee for Weights and Measures – Mutual Recognition Arrangement), or supplementary comparisons, for the establishment of the International System of Units (SI). The recent result regarding $^{131}\text{I}$, a targeted radiotherapy radionuclide, in the key comparison type K1, within the BIPM-International Reference System (SIR), is presented in the paper [21].

5. NATIONAL TRACEABILITY FOR MEDICAL RADIONUCLIDES

Establishment of the national traceability was performed in two steps: (i) calibration of the secondary standard, ionization chamber, CENTRONIC IG12/20A; (ii) calibration of commercial radionuclide calibrators and check of the agreement between the measurements and the reference (conventionally true value) activity.

5.1. CALIBRATION OF THE IONISATION CHAMBER CENTRONIC IG12/20A

The operation was performed using standard solutions, prepared and standardized absolutely in RML. It consisted from the determination of the response value, expressed as the ratio between the ionisation current, in pA, and activity, in MBq, determined for various recipients, containing 2 ml; 3.6 ml and 5 ml of solution and were compared with the theoretically calculated values, based on other radionuclides measurements, and the key comparison reference values (KCRV), when possible. Table 6 presents the results from [12, 22].
Table 6
CENTRONIC IG12/20A calibration figures for medical radionuclides

<table>
<thead>
<tr>
<th>Radio nuclide</th>
<th>$F_{2}$, pA MBq$^{-1}$ 2 mL vial</th>
<th>$F_{3.6}$, pA MBq$^{-1}$ 3.6 mL vial</th>
<th>$F_{5}$, pA MBq$^{-1}$ 5 mL vial</th>
<th>Calculated $F_{7}$, pA MBq$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{64}$Cu</td>
<td>-</td>
<td>-</td>
<td>6.302 ±1.5%</td>
<td>6.25 ± 3%</td>
</tr>
<tr>
<td>$^{68}$Ga</td>
<td>-</td>
<td>-</td>
<td>31.81 ± 0.6%</td>
<td>32.06 ± 3%</td>
</tr>
<tr>
<td>$^{99m}$Tc</td>
<td>6.738 ± 1.0 %</td>
<td>-</td>
<td>6.658 ± 3.0 %$^{a}$</td>
<td>6.650 ± 2.1%$^{b}$</td>
</tr>
<tr>
<td>$^{131}$I</td>
<td>13.20 ± 0.52 %</td>
<td>13.12 ± 0.33 %</td>
<td>13.10 ± 0.18% (KCRV)</td>
<td>12.99 ± 0.43%</td>
</tr>
<tr>
<td>$^{153}$Sm</td>
<td></td>
<td>2.53 ± 1.5 %</td>
<td>2.43 ± 3%</td>
<td></td>
</tr>
<tr>
<td>$^{177}$Lu</td>
<td>1.560±0.5% (KCRV)</td>
<td>1.533 ±1.1 %</td>
<td>1.57 ±3%</td>
<td></td>
</tr>
<tr>
<td>$^{186}$Re</td>
<td>1.155 ± 1.0 %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{188}$Re</td>
<td>2.52 ± 1.0 %</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Legend: $^{a,b}$) two different methods

5.2. CALIBRATION OF COMMERCIAL RADIONUCLIDE CALIBRATORS


The most used commercial radionuclide calibrators in Romanian nuclear medicine units are Curiementor 3, ¾, 4 and Capintec CRC 15, 25 R. Our role is to remeasure the activity of a solution, standardized with the calibrated CENTRONIC IG12/20A ionization chamber, using the provider’s dial setting of the device, and to compare the indicated activity with the reference value. Two situations can occur: (a) The difference from reference activity is higher than ± 10 % and then the calibration factor (dial setting) is modified. When the adjustment is not possible, the value of the correction factor to be applied is written in the certificate. (b) The obtained value differs from the reference one by less than ± 10 % and the statement that the values agree within the uncertainties interval is done. Table 7 presents the results, expressed as differences from the calibrator measured activity and reference, IFIN-HH, RML value, for a P6 vial type, containing 5 ml of solution [8].
Table 7

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Curientor</th>
<th>Capintec CRC-15, 25 R</th>
<th>Other calibrators</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc</td>
<td>-3.6%</td>
<td>+3.1%</td>
<td>Adjusted Picker: -0.7%</td>
</tr>
<tr>
<td>$^{131}$I</td>
<td>-2.7%</td>
<td>-0.8%</td>
<td>Adjusted Picker: +0.9%</td>
</tr>
</tbody>
</table>

6. CONCLUSIONS

– The RML developed absolute methods for the standardization of the most used medical radionuclides, especially for PET and therapy uses, and validated them in international comparisons.
– The decay scheme parameters of some new radionuclides were studied as a contribution at the creation of the international decay data bases.
– Various methods, for specific radionuclides, were used for the control of radionuclide purity.
– The laboratory assured the entire metrological chain from the international system of units (SI) up to the end users, radiopharmaceutical production units and hospitals.

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REFERENCES


