Activity measurements of the radionuclides ^{18}F and ^{64}Cu for the NIST, USA in the ongoing comparisons BIPM.RI(II)-K4.F-18 and BIPM.RI(II)-K4.Cu-64

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Abstract

In 2016, comparisons of activity measurements of ^{18}F and ^{64}Cu using the Transfer Instrument of the International Reference System (SIRTI) took place at the National Institute of Standards and Technology (NIST, USA). This is the first SIRTI comparison for ^{64}Cu. Ampoules containing about 27 kBq of ^{18}F and 100 kBq of ^{64}Cu solutions were measured in the SIRTI for about 5 and 1.5 half-lives, respectively. The NIST standardized the activity in the ampoules by ionization chamber measurements traceable to 4π(LS)$\beta-\gamma$ anticoincidence measurements. The comparisons, identifiers BIPM.RI(II)-K4.F-18 and BIPM.RI(II)-K4.Cu-64, are linked to the corresponding BIPM.RI(II)-K1.F-18 and BIPM.RI(II)-K1.Cu-64 comparisons and degrees of equivalence with the respective key comparison reference values have been evaluated. The NIST replaces its earlier degree of equivalence for ^{18}F obtained in the frame of the CCRI(II)-K3.F-18 comparison in 2001.

1. Introduction

Radionuclides are essential for nuclear medicine where short-lived (often much less than one day) radionuclides are used, particularly for imaging. The use of nuclear medicine is increasing with the accessibility of these radionuclides which are consequently of great interest to the National Metrology Institutes (NMIs) in terms of standardization and SI traceability. However, sending ampoules of short-lived radioactive material to the Bureau International des Poids et Mesures (BIPM) for measurement in the International Reference System (SIR) [1] is only practicable for the NMIs that are based in Europe. Consequently, to extend the utility of the SIR and enable other NMIs to participate, a transfer instrument (SIRTI) has been developed at the BIPM with the support of the Consultative Committee for Ionizing Radiation CCRI(II) Transfer Instrument Working Group [2].

The BIPM ongoing K4 comparisons of activity measurements of ^{18}F (half-life $T_{1/2}$ = 1.8288 h; u = 0.0003 h [3])[1] and of ^{64}Cu (half-life of 12.7004(20) h [4]) are based on the SIRTI, a well-type NaI(Tl) crystal calibrated against the SIR, which is moved to each participating laboratory. The stability of the system is monitored using a ^{94}Nb reference source (half-life of 20 300(1 600) years [5]) from the Joint Research Centre of the European Commission (JRC, Geel), which also contains the ^{93m}Nb isotope. The ^{18}F or ^{64}Cu count rate above a low-energy threshold, defined by the ^{93m}Nb x-ray peak at 16.6 keV, is measured relative to the ^{94}Nb count rate above the same threshold. Once the threshold is set, a brass liner is placed in the well to suppress the ^{93m}Nb contribution to the ^{94}Nb stability measurements. It should be noted that the uncertainty associated with the ^{94}Nb decay correction is negligible. The ^{18}F or ^{64}Cu SIR ampoule is placed in the detector well in a PVC (polyvinyl chloride) liner to stop the β^+ particles while minimizing the production of bremsstrahlung. No extrapolation to zero energy is carried out as all the measurements are made with the same threshold setting. The live-time technique using the MTR2 module from the Laboratoire National d'Essais – Laboratoire National Henri Becquerel, France (LNE-LNHB) [6] is used to correct for dead-time losses, taking into account the width of the oscillator pulses. The standard uncertainty associated with the live-time correction, due to the effect of finite frequency of the oscillator, is negligible.

Similarly to the SIR, a SIRTI equivalent activity A_E is deduced from the ^{18}F or ^{64}Cu and the ^{94}Nb counting results and the ^{18}F or ^{64}Cu activity measured by the NMI: A_E is inversely proportional to the detection efficiency, i.e. A_E is the activity of the source measured by the participant divided by the ^{18}F or ^{64}Cu count rate in the SIRTI relative to the ^{94}Nb count rate. The possible presence of impurity in the solution should be accounted for using γ-spectrometry measurements carried out by the NMI.

The present K4 comparisons are linked to the corresponding BIPM.RI(II)-K1 comparisons through the calibration of the SIRTI against the SIR at the BIPM and, consequently, the degrees of equivalence with the K1 key comparison reference value (KCRV) can be evaluated. The K4 ^{18}F comparison results based on primary measurements carried out by the NMI, or ionization chamber measurements traceable to primary ^{18}F measurements made within one year prior to the K4 comparison, are eligible for inclusion in the KCRV.

The protocol [7] and previous comparison results for the BIPM.RI(II)-K4 comparisons are available in the key comparison database of the CIPM (International Committee on Weights and Measures) Mutual Recognition Arrangement [8]. Publications concerning the details of the SIRTI and its calibration against the SIR can be found elsewhere [9, 10].

2. Participants

As detailed in the protocol, participation in the BIPM.RI(II)-K4 comparisons mainly concerns member states that are located geographically far from the BIPM and that have developed a primary measurement method for the radionuclide of concern. However, at the time of the comparison, the National Metrology Institute (NMI) may decide for convenience to use a secondary method, for example a calibrated ionization chamber. In this case, the traceability of the calibration needs to be clearly identified.

[1] Hereafter, the last digits of the standard uncertainties are given in parenthesis.

The present comparisons took place at the National Institute of Standards and Technology (NIST), USA, in May 2016, who used an ionization chamber calibrated by the 4π(LS)β–γ anticoincidence method nine months and two months prior to the comparison of the ^{18}F and ^{64}Cu solutions, respectively.

3. The SIRTI at the NIST

The reproducibility and stability of the SIRTI at the NIST were checked by measuring the count rate produced by the reference ^{94}Nb source No. 1, the threshold position (defined by the ^{93m}Nb x-ray peak), the background count rate, the frequency of the oscillator No. 1 for the live-time correction and the room temperature as shown in Figure 1. The plots shown in the Figure represent the differences from the values indicated in the figure caption, using the appropriate units, as given, for each quantity measured.

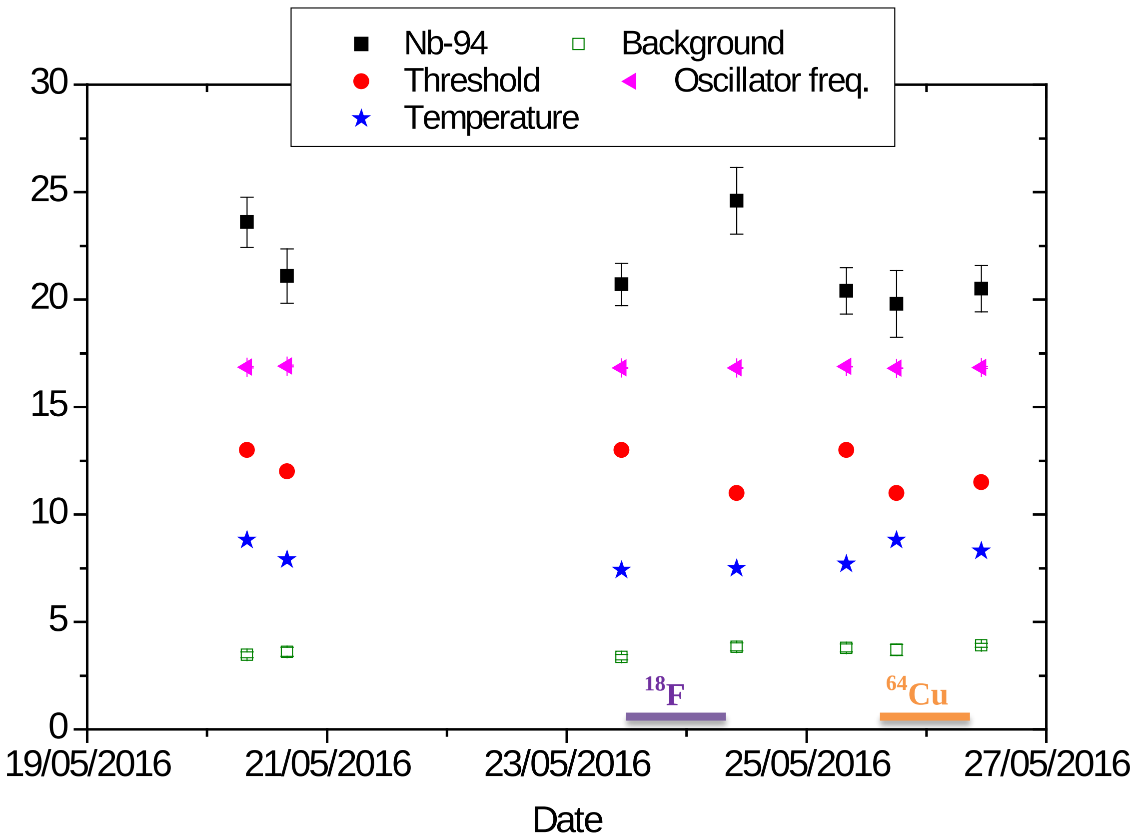


Figure 1: Fluctuation of the SIRTI at the NIST. Black squares: ^{94}Nb No.1 count rate / s^{-1} above 8470 s^{-1}; triangles: frequency of the oscillator No.1 / Hz above 999 985 Hz; circles: threshold position / channel above 85 channels; stars: room temperature / °C above 15 °C; open squares: background count rate / s^{-1} above 20 s^{-1}. Statistical uncertainty (k = 1) for the Nb source, background and oscillator counts are shown (in some cases the uncertainties are not visible in the plot as they hidden by the character printed for the data point).

The SIRTI was stable during the comparison, with some fluctuation in the ^{94}Nb count rate uncorrelated with the threshold position. The background was very stable and about a factor three lower than the background observed at the BIPM. Individual ^{94}Nb results were used to normalize the ^{18}F and ^{64}Cu count rates. The mean ^{94}Nb No. 1 count rate, corrected for live-time, background, and decay, measured at the NIST was 8491.3(6) s^{-1}, which slightly differs from the weighted mean since the set-up of the system in March 2007, 8492.82(23) s^{-1} and this is taken into account in the uncertainty evaluation of the comparison result. Finally, the ^{94}Nb count rate was checked on the return of the SIRTI to the BIPM after the NIST comparison, giving a value of 8490.8(14) s^{-1} in agreement with the measurements carried out at the NIST.

4. The ^{18}F and ^{64}Cu solutions standardized at the NIST

The ^{18}F and ^{64}Cu solutions measured in the SIRTI are described in Table 1, including any impurities, when present, as identified by the laboratory. Two SIR ampoules were prepared from each solution for measurement in the SIRTI. The density and volume of the solutions in the ampoules conformed to the K4 protocol requirements. No drops of solution were observed in the ampoules which had been centrifuged.

Table 1: Characteristics of the solutions measured in the SIRTI

Radionuclide	**Solvent / mol dm^{-3}**	**Carrier / µg g^{-1}**	**Density at 20 °C / g cm^{-3}**	**Ampoule number**	**Mass / g**	**Impurity***
^{18}F (FDG)	water	–	1.00	1	3.565 96	–
				2	3.62207	–
^{64}Cu	HCl / 0.1	Cu^{2+} / 15.8	1.00	1	3.568 29	^{56}Co: 3.15(19) × 10^{-8} ^{57}Co: 9.58(48) × 10^{-7} ^{58}Co: 2.82(31) × 10^{-7}
				2	3.578 64	

* Ratio of the impurity activity to the main radionuclide activity at the reference date

The ^{18}F and ^{64}Cu activities in the SIRTI ampoules were deduced from the measurement at the NIST of each master solution in a well-type ionization chamber (IC) and a dilution factor of 44.70(2) and 47.02(3), respectively. The IC had been calibrated for ^{18}F and ^{64}Cu, nine months and two months respectively prior to the K4 comparison, by the 4π(LS)β-γ coincidence method (LTAC). The ^{18}F LTAC measurements, carried out in August, 2015, were consistent with the most recent NIST standard [18], and differed by 4 % from the earlier NIST standards [19]. The ^{64}Cu LTAC measurements are described in detail in a manuscript being prepared for publication [20].

The measurement results are summarized in Tables 2 and 3 while the uncertainty budgets of the NIST primary measurements are given in appendix 2.

Table 2: The ^{18}F and ^{64}Cu standardizations by the NIST

Radionuclide	Measurement method ACRONYM*	Activity conc. / kBq g^{-1}	Standard uncert. / kBq g^{-1}	Reference date YYYY-MM-DD	Half-life used by the NMI / h
^{18}F	IC calibrated 4P-IC-GR-00-00-00 in August 2015 by 4π(LS)β-γ anticoinc. (LTAC) 4P-LS-BP-NA-GR-AC	7.500	0.030	2016-05-23 17:00 UTC	1.828 90(23)
^{64}Cu	IC calibrated 4P-IC-GR-00-00-00 in March 2016 by 4π(LS)β-γ anticoinc. (LTAC) 4P-LS-BP-NA-GR-AC	28.96	0.17	2016-05-25 17:00 UTC	12.7004(20)

* See appendix 1

5. The ^{18}F and ^{64}Cu measurements in the SIRTI at the NIST

The maximum live-time corrected count rate in the NaI(Tl) was 15 000 s^{-1}, which conforms to the limit of 20 000 s^{-1} set in the protocol [7]. In addition, a relative standard uncertainty of 2×10^{-4} and 2.5×10^{-4} for ^{18}F and ^{64}Cu respectively, was added to take account of a possible drift in the SIRTI at high count rate [9]. The time of each SIRTI measurement was obtained from the manual synchronization of the SIRTI laptop with another computer connected to a local NTP time server. An additional relative standard uncertainty of 1×10^{-4} has been included for ^{18}F to take account of a 1 s uncertainty in the measurement time.

In principle, the live-time correction should be modified to take into account the decaying count rate [11]. In the present experiments, the duration of the measurements made at high rate has been limited to 400 s and 1000 s for ^{18}F and ^{64}Cu respectively, so that the relative effect of decay on the live-time correction is less than one part in 10^4.

Two ampoules of each of the ^{18}F and ^{64}Cu solutions were measured alternatively for 5 and 1.5 half-lives, respectively, and the results are shown in Figures 2a and 2b. The last 14 measurements shown in Figure 2a were not used for the comparison as the count rate in the SIRTI was lower than 1000 s^{-1}. The reduced chi-squared values evaluated for these series of measurements are 1.14 and 0.78 for ^{18}F and ^{64}Cu, respectively, showing that the data are consistent. The absence of significant trend confirms the stability and adequate live-time correction of the SIRTI, as well as the absence of significant impurity in the solutions.

The uncertainty budgets for the SIRTI measurements of the ^{18}F and ^{64}Cu ampoules are given in Table 4a and 4b. As the decay scheme of ^{64}Cu is similar to the one of ^{18}F, no further

Monte-Carlo simulations were carried out for ^{64}Cu and the results obtained for ^{18}F were used in the uncertainty evaluation. Further details are given in reference [9].

Table 3: The NIST uncertainty budgets for the IC activity measurement of the ^{18}F and ^{64}Cu ampoules (May 2016)

Uncertainty contributions due to	**Evaluation method**	**^{18}F**		**^{64}Cu**	
		Relative std uncert. × 10^4	**Comments**	**Relative std uncert. × 10^4**	**Comments**
Ampoule to RRS[2] ratio	A	2	Average std deviation, 90 meas. of ^{18}F, 108 meas. of RRS 50	2	Average std deviation, 82 or 90 meas. of ^{64}Cu on each of the two ampoules, 108 meas. of RRS 50
Activity estimation	A	0.5	Std deviation of the estimation in each of two ampoules	0.5	Std deviation of the estimation in each of two ampoules
RRS ratio, 1000 to 50	B	7	Uncertainty attending the ratio between RRS 1000, used in the calib. of the IC, and RRS 50, used in this meas.	–	Not required; both the calibration and this meas. used RRS 50.
Weighing	B	7	Mass of solution in the ampoules	7	Mass of solution in the ampoules
Dilution factor	B	5		6	
Background	A	0.09*	228 measurements	0.09*	142 measurements
Decay correction	B	0.4	From uncert. for ^{18}F half-life	0.1	From uncert. for ^{64}Cu half-life
Calibration factor of IC (see appendix 2)	B	38	Calibration by LTAC in August 2015	58	Calibration by LTAC in March 2016
Impurities	B	–		0.01	
Relative combined std uncertainty		40		59	

* Included in the first uncertainty component (ampoule to RRS ratio)

[2] Radium Reference Source

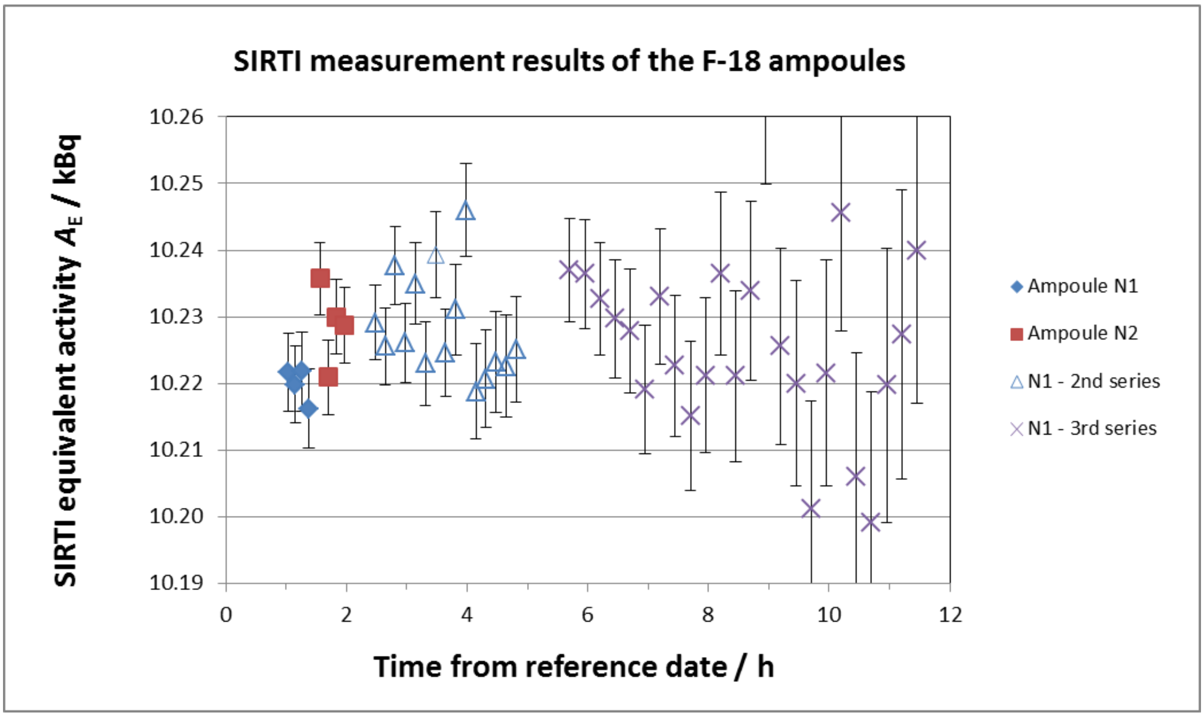


Figure 2a: The ^{18}F measurement results in the SIRTI at the NIST. The uncertainty of the ^{18}F activity concentration, which is constant over all the measurements, is not included in the uncertainty bars shown on the graph. The last 14 measurements were not used in the analysis. See text.

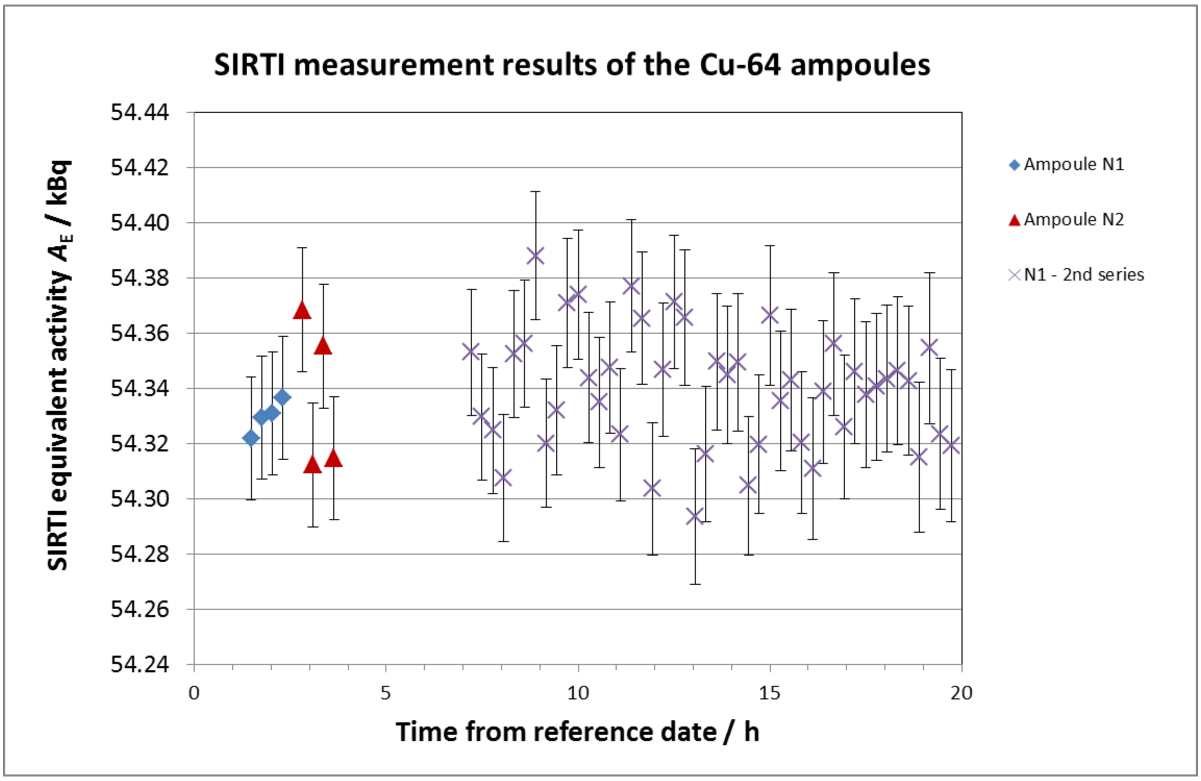


Figure 2b: As for Figure 2a, but for the ^{64}Cu. All measurements were used in the analysis.

Table 4a: Uncertainty budgets for the SIRTI measurement of the ^{18}F ampoules

Uncertainty contributions due to	Comments	Evaluation method	Relative standard uncert. × 10^4
^{18}F to ^{94}Nb meas. ratio including live-time, background, decay corrections and threshold setting	Standard uncertainty of the weighted mean of 33 measurements, taking into account the correlation due to the ^{18}F half-life	A	2.4
Long-term stability of the SIRTI	Weighted standard deviation of 85 series, each series consisting of 10 measurements	A	0.3
Nb-1 bias from the mean since 2007	Relative difference from the mean	B	1.8
Effect of decay on the live-time correction	Maximum measurement duration evaluated from [12]	B	< 1
SIRTI drift at high count rate	Mean possible drift over all ^{18}F measurements at the NIST.	B	2
Ampoule dimensions	From the IRMM report [13] and sensitivity coefficients from Monte-Carlo simulations	B	2*
Ampoule filling height	Solution volume is 3.6(1) cm^3; sensitivity coefficients from Monte-Carlo simulations	B	2*
Solution density	Between 1 g/cm^3 and 1.01 g/cm^3 as requested in the protocol; sensitivity coefficients from Monte-Carlo simulations	B	0.7
Measurement time	1 s uncertainty	B	1
Relative combined standard uncertainty			3.9

***** Included in the type A uncertainty of the measurements of two ampoules of ^{18}F

Table 4b: Uncertainty budgets for the SIRTI measurement of the ^{64}Cu ampoules

Uncertainty contributions due to	**Comments**	**Evaluation method**	**Relative standard uncert. × 10^4**
^{64}Cu to ^{94}Nb meas. ratio meas. including live-time, background, decay corrections and threshold setting	Standard uncertainty of the weighted mean of 54 measurements, taking into account the correlation due to the ^{64}Cu half-life	A	1.2
Long-term stability of the SIRTI	Weighted standard deviation of 85 series, each series consisting of 10 measurements	A	0.3
Nb-1 bias from the mean since 2007	Relative difference from the mean	B	1.8
Effect of decay on the live-time correction	Maximum measurement duration evaluated from [12]	B	< 1
SIRTI drift at high count rate	Mean possible drift over all ^{99m}Tc measurements at the NIST.	B	2.5
Ampoule dimensions	From the IRMM report [13] and sensitivity coefficients from Monte-Carlo simulations	B	2*
Ampoule filling height	Solution volume is 3.6(1) cm^3; sensitivity coefficients from Monte-Carlo simulations	B	2
Solution density	Between 1 g/cm^3 and 1.01 g/cm^3 as requested in the protocol; sensitivity coefficients from Monte-Carlo simulations	B	0.7
Impurities	Negligible effect on the SIRTI measurements	B	0
Relative combined standard uncertainty			4.2

***** Included in the type A uncertainty of the measurements of two ampoules of ^{64}Cu

6. Comparison results and degrees of equivalence

The weighted mean and uncertainty of all the measured A_E values is calculated taking into account correlations. The standard uncertainty $u(A_E)$ is obtained by adding in quadrature the SIRTI combined uncertainty from Tables 4a and 4b and the uncertainty stated by the participant for the ^{18}F and ^{64}Cu measurements (see Table 2). The correlation between the NIST and the BIPM due to the use of the same ^{64}Cu half-life is negligible in view of the small contribution of this half-life to the combined uncertainty of the measurements.

The K4 comparison results are given in Table 5 as well as the linked results A_e in the corresponding BIPM.RI(II)-K1 comparisons which were obtained by multiplying A_E by the linking factors L = 1495.1(18) for ^{18}F and 1482.2(25) for ^{64}Cu. The ^{64}Cu linking factor has been obtained recently through the measurement of ^{64}Cu ampoules from the CNRS/CEMHTI (Orléans, in 2015) and the NPL (Teddington, in 2016) in both the SIRTI and the SIR. The solutions probably contained small amounts of ^{67}Cu giving rise to impurity corrections to the SIRTI measurements of a few parts in 1000 at the end of about 35 hours of measurements. The linking factors obtained are 1479.1(18) and 1483.8(15), for the CNRS and NPL solutions respectively, giving a weighted mean result of 1482.2(25) taking correlations into account [10].

Table 5: BIPM.RI(II)-K4. comparison results and link to the BIPM.RI(II)-K1 comparisons

Radionuclide	**Measurement method** ACRONYM*	**Solution volume (calculated) /cm³**	**A_E /kBq**	**$u(A_E)$ /kBq**	**Linked A_e /kBq**	**$u(A_e)$ /kBq**
^{18}F	IC calibrated 4P-IC-GR-00-00-00 in August 2015 by 4π(LS)β-γ anticoinc. (LTAC) 4P-LS-BP-NA-GR-AC	3.57 and 3.62	10.228	0.041	15 291	64
^{64}Cu	IC calibrated 4P-IC-GR-00-00-00 in March 2016 by 4π(LS)β-γ anticoinc. (LTAC) 4P-LS-BP-NA-GR-AC	3.57 and 3.58	54.34	0.32	80 540	500

* See appendix 1

Every participant in the K4 comparison is entitled to have one result included in the key comparison database (KCDB) as long as the laboratory is a signatory or designated institute listed in the CIPM MRA. Normally, the most recent result is the one included. Any participant may withdraw its result only if all the participants agree.

The KCRVs for ^{18}F and ^{64}Cu have been defined in the frame of the BIPM.RI(II)-K1.F-18 and BIPM.RI(II)-K1.Cu-64 comparisons using direct contributions to the SIR, and are equal to 15 276(24) kBq [14] and 80 990(340) kBq [15], respectively.

The degree of equivalence of a particular NMI, i, with the KCRV is expressed as the difference D_i with respect to the KCRV

$$D_i = A_{\mathrm{e}i} - \mathrm{KCRV} \qquad (1)$$

and the expanded uncertainty (k = 2) of this difference, U_i , known as the equivalence uncertainty, hence

$$U_i = 2u(D_i), \qquad (2)$$

taking correlations into account as appropriate [16].

The degree of equivalence between any pair of NMIs, i and j, is expressed as the difference D_{ij} in their results

$$D_{ij} = D_i - D_j = A_{\mathrm{e}i} - A_{\mathrm{e}j} \qquad (3)$$

and the expanded uncertainty of this difference U_{ij} where

$$U_{ij}^2 = 4u^2(D_{ij}) = 4\left[u_i^{\,2} + u_j^{\,2} - 2u(A_{\mathrm{e}i}, A_{\mathrm{e}j})\right] \qquad (4)$$

where any obvious correlations between the NMIs (such as a traceable calibration) are subtracted using the covariance $u(A_{ei}, A_{ej})$, as is the correlation coming from the link of the SIRTI to the SIR. The covariance between two participants in the K4 comparison is given by

$$u(A_{ei}, A_{ej}) = A_{ei}\, A_{ej}\, (u_L / L)^2 \qquad (5)$$

where u_L is the standard uncertainty of the linking factor L given above. However, the CCRI decided in 2011 that these pair-wise degrees of equivalence no longer need to be published as long as the methodology is explained.

Tables 6a and 6b show the matrices of the degrees of equivalence with the KCRV as they will appear in the KCDB. It should be noted that for consistency within the KCDB, a simplified level of nomenclature is used with A_{ei} replaced by x_i. The introductory text is that agreed for the comparison. The graph of the degrees of equivalence with respect to the KCRV (identified as x_R in the KCDB), is shown in Figure 3a and Figure 3b. The graphical representation indicates in part the degree of equivalence between the NMIs but obviously does not take into account the correlations between the different NMIs.

With the present comparison, the NIST updated its degree of equivalence for the activity measurement of ^{18}F. A shift of +4.1 % is observed when comparing with the earlier degree of equivalence in the CCRI(II)-K3.F-18 comparison in 2001 [17]. This confirms independently the change of 4.0 % observed by the NIST in its ^{18}F primary measurements in 2014 [18].

Conclusion

In 2016, the NIST (USA) hosted the SIRTI to participate in the BIPM ongoing key comparison for activity measurement of ^{18}F (BIPM.RI(II)-K4.F-18) and was the first participant in the BIPM.RI(II)-K4.Cu-64 comparison. These K4 comparisons are linked to the corresponding BIPM.RI(II)-K1.F-18 and BIPM.RI(II)-K1.Cu-64 comparisons and degrees of equivalence with the respective key comparison reference values defined in the frame of the K1 comparisons have been evaluated. The NIST greatly improves its earlier degree of equivalence for ^{18}F obtained in the frame of the CCRI(II)-K3.F-18 comparison in 2001. The NIST linked result in the BIPM.RI(II)-K1.Cu-64 comparison agrees with the KCRV, indicating that the SIRTI was linked to the SIR successfully. The degrees of equivalence have been approved by the CCRI(II) and are published in the BIPM key comparison database.

Other results may be added when other NMIs contribute with ^{18}F and ^{64}Cu activity measurements to the K4 or K1 comparisons or take part in other linked Regional Metrology Organization comparisons. It should be noted that the final data in this paper, while correct at the time of publication, will become out-of-date as NMIs make new comparisons. The formal results under the CIPM MRA [7] are those available in the KCDB.

Table 6a. Introductory text and table of degrees of equivalence for ^{18}F

Key comparison BIPM.RI(II)-K1.F-18

MEASURAND : **Equivalent activity of ^{18}F**

Key comparison reference value: the SIR reference value for this radionuclide is x_R = 15 276 kBq
with a standard uncertainty, u_R = 24 kBq (see Section 4.1 of the Final Report [14]). The value x_i is the equivalent activity for laboratory *i*.

The degree of equivalence of each laboratory with respect to the reference value is given by a pair of terms:
$D_i = (x_i - x_R)$ and U_i, its expanded uncertainty (k = 2), both expressed in MBq, and
$U_i = 2((1 - 2w_i)u_i^2 + u_R^2)^{1/2}$ where w_i is the weight of laboratory *i* contributing to the calculation of x_R.

Linking BIPM.RI(II)-K4.F-18 to BIPM.RI(II)-K1.F-18

The value x_i is the SIRTI equivalent activity for laboratory *i* participant in BIPM.RI(II)-K4.F-18
multiplied by the linking factor to BIPM.RI(II)-K1.F-18 (see [10]).

The degree of equivalence of laboratory *i* participant in BIPM.RI(II)-K4.F-18 with respect to the key comparison reference value is given
by a pair of terms: $D_i = (x_i - x_R)$ and U_i, its expanded uncertainty (k = 2), both expressed in MBq.
The approximation $U_i = 2(u_i^2 + u_R^2)^{1/2}$ is used in the following table as none of these laboratories contributed to the KCRV.

Linking CCRI(II)-K3.F-18 to BIPM.RI(II)-K1.F-18

The value x_i is the equivalent activity for laboratory *i* participant in CCRI(II)-K3.F-18
having been normalized to the value of the NPL and the LNE-LNHB (2002) combined as the link (see [17]).

The degree of equivalence of laboratory *i* participant in CCRI(II)-K3. with respect to the key comparison reference value is given
by a pair of terms: $D_i = (x_i - x_R)$ and U_i, its expanded uncertainty (k = 2), both expressed in MBq.
The approximation $U_i = 2(u_i^2 + u_R^2)^{1/2}$ is used in the following table as none of these laboratories contributed to the KCRV.

Linking APMP.RI(II)-K3.F-18 to BIPM.RI(II)-K1.F-18

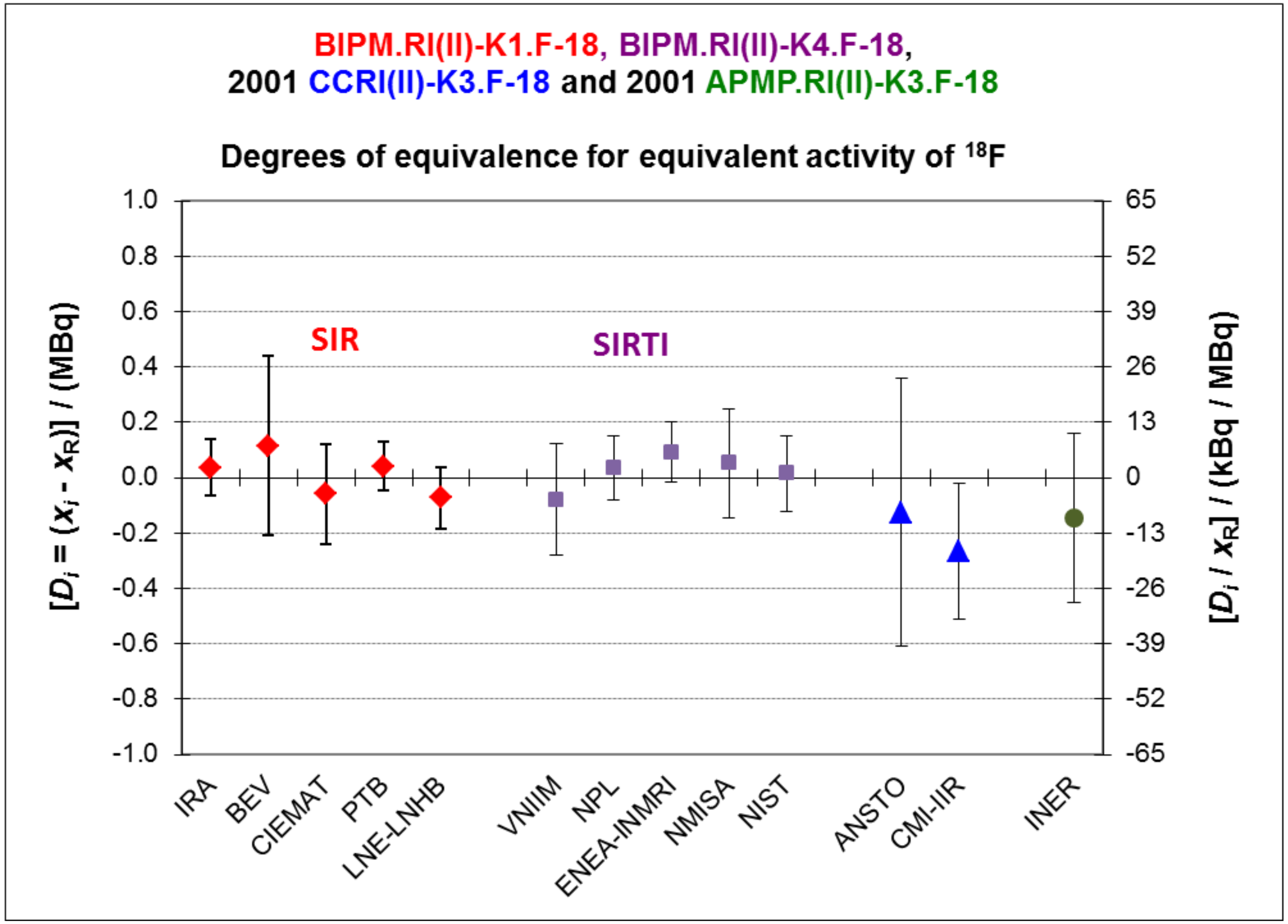
The value x_i is the equivalent activity for laboratory *i* participant in APMP.RI(II)-K3.F-18
having been normalized to the value of the NPL and the LNE-LNHB (2002) combined as the link (see [17]).

The degree of equivalence of laboratory *i* participant in APMP.RI(II)-K3. with respect to the key comparison reference value is given by a pair of terms: $D_i = (x_i - x_R)$ and U_i, its expanded uncertainty (k = 2), both expressed in MBq.
The approximation $U_i = 2(u_i^2 + u_R^2)^{1/2}$ is used in the following table as this laboratory did not contribute to the KCRV.

These statements make it possible to extend the BIPM.RI(II)-K1.F-18 matrices of equivalence to all participants in the CCRI(II)-K3.F-18, the APMP.RI(II)-K3.F-18 and the BIPM.RI(II)-K4.F-18 comparisons.

Lab *i*	D_i / MBq	U_i / MBq
IRA	**0.04**	0.10
BEV	**0.11**	0.32
CIEMAT	**-0.06**	0.18
PTB	**0.04**	0.09
LNE-LNHB	**-0.07**	0.11
VNIIM	**-0.08**	**0.20**
NPL	**0.04**	**0.11**
ENEA-INMRI	**0.09**	**0.11**
NMISA	**0.05**	**0.20**
NIST	**0.02**	**0.14**
ANSTO	**-0.13**	0.48
CMI-IIR	**-0.27**	0.24
NIST	**-0.61**	0.32
INER	**-0.15**	0.30

Figure 3a. Graph of degrees of equivalence with the KCRV for ^{18}F
(as it appears in Appendix B of the MRA)



N.B. The right-hand axis gives approximate relative values only

Table 6b. Table of degrees of equivalence and introductory text for ^{64}Cu

Key comparison BIPM.RI(II)-K1.Cu-64

MEASURAND : Equivalent activity of ^{64}Cu

**Key comparison reference value: the SIR reference value x_R for this radionuclide is 80.99 MBq,
with a standard uncertainty u_R of 0.34 MBq.
The value x_i is taken as the equivalent activity for laboratory *i*.**

**The degree of equivalence of each laboratory with respect to the reference value is given by a pair of terms:
$D_i = (x_i - x_R)$ and U_i, its expanded uncertainty (k = 2), both expressed in MBq, and
$U_i = 2((1 - 2w_i)u_i^2 + u_R^2)^{1/2}$ when each laboratory has contributed to the calculation of x_R.**

Linking BIPM.RI(II)-K4.Cu-64 to BIPM.RI(II)-K1.Cu-64

**The value x_i is the SIRTI equivalent activity for laboratory *i* participant in BIPM.RI(II)-K4.Cu-64
multiplied by the linking factor to BIPM.RI(II)-K1.Cu-64 (see Section 6 of Final Report).**

**The degree of equivalence of laboratory *i* participant in BIPM.RI(II)-K4.Cu-64 with respect to the key comparison reference value is given
by a pair of terms: $D_i = (x_i - x_R)$ and U_i, its expanded uncertainty (k = 2), both expressed in MBq.
The approximation $U_i = 2(u_i^2 + u_R^2)^{1/2}$ is used in the following table.**

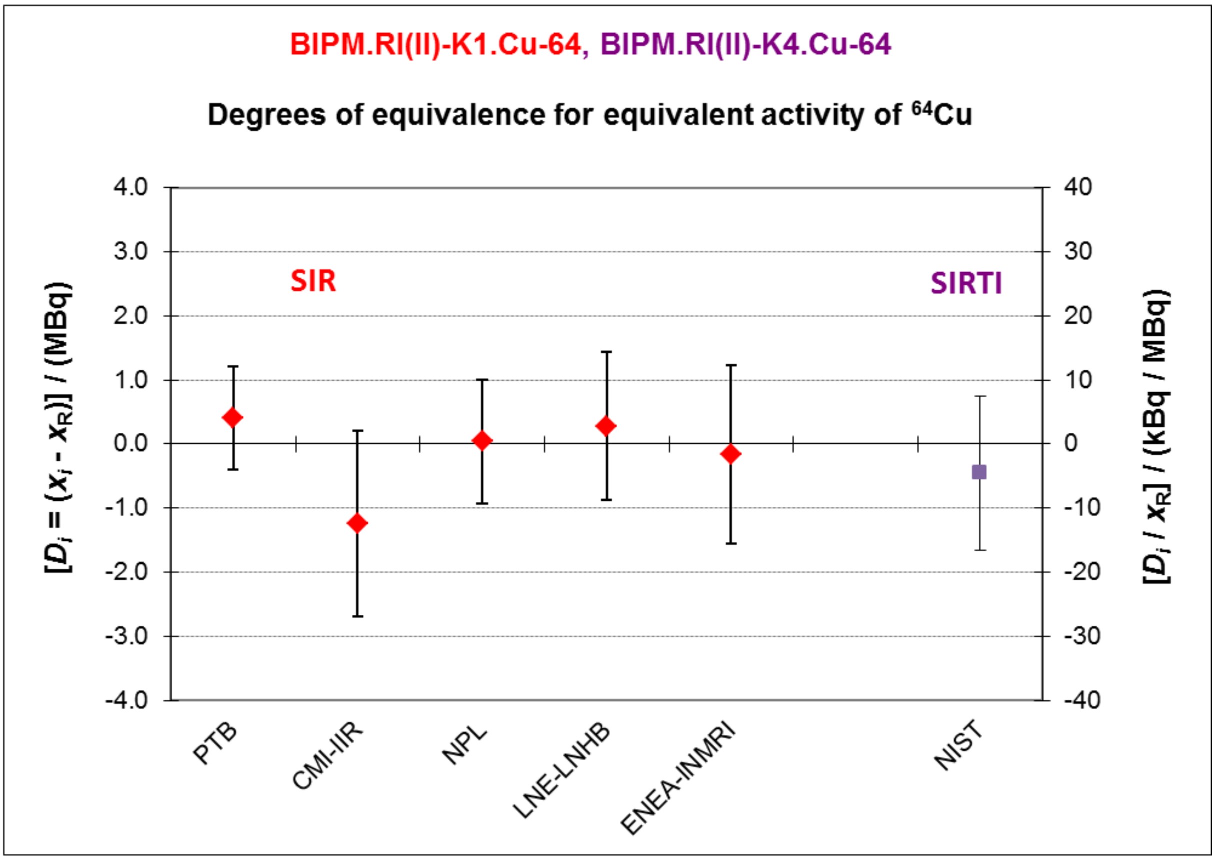
**These statements make it possible to extend the BIPM.RI(II)-K1.Cu-64 matrices of equivalence
to all participants in the BIPM.RI(II)-K4.Cu-64 comparisons.**

Table 6b continued. Degrees of equivalence for ^{64}Cu

Lab *i* ⇩

	D_i / MBq	U_i
PTB	**0.4**	0.8
CMI-IIR	**-1.2**	1.4
NPL	**0.0**	1.0
LNE-LNHB	**0.3**	1.2
ENEA-INMRI	**-0.2**	1.4
NIST	**-0.4**	**1.2**

Figure 3b. Graph of degrees of equivalence with the KCRV for ^{64}Cu
(as it appears in Appendix B of the MRA)



N.B. The right-hand axis gives approximate relative values only

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Appendix 1. **Acronyms used to identify different measurement methods**

Each acronym has six components, geometry-detector (1)-radiation (1)-detector (2)-radiation (2)-mode. When a component is unknown, ?? is used and when it is not applicable 00 is used.

Geometry	**acronym**	**Detector**	**acronym**
4π	4P	proportional counter	PC
defined solid angle	SA	press. prop. counter	PP
2π	2P	liquid scintillation counting	LS
undefined solid angle	UA	NaI(Tl)	NA
		Ge(HP)	GH
		Ge(Li)	GL
		Si(Li)	SL
		CsI(Tl)	CS
		ionization chamber	IC
		grid ionization chamber	GC
		Cerenkov light detector	LC
		calorimeter	CA
		solid plastic scintillator	SP
		PIPS detector	PS

Radiation	**acronym**	**Mode**	**acronym**
positron	PO	efficiency tracing	ET
beta particle	BP	internal gas counting	IG
Auger electron	AE	CIEMAT/NIST	CN
conversion electron	CE	sum counting	SC
mixed electrons	ME	coincidence	CO
bremsstrahlung	BS	anti-coincidence	AC
gamma rays	GR	coincidence counting with efficiency tracing	CT
X - rays	XR	anti-coincidence counting with efficiency tracing	AT
photons (x + γ)	PH	triple-to-double coincidence ratio counting	TD
alpha - particle	AP	selective sampling	SS
mixture of various radiations	MX	high efficiency	HE

Examples

Method	**acronym**
4π(PC)β–γ-coincidence counting	4P-PC-BP-NA-GR-CO
4π(PPC)β–γ-coincidence counting eff. trac.	4P-PP-MX-NA-GR-CT
defined solid angle α-particle counting with a PIPS detector	SA-PS-AP-00-00-00
4π(PPC)AX-γ(Ge(HP))-anticoincidence counting	4P-PP-MX-GH-GR-AC
4π CsI-β,AX,γ counting	4P-CS-MX-00-00-HE
calibrated IC	4P-IC-GR-00-00-00
internal gas counting	4P-PC-BP-00-00-IG

Appendix 2. **Uncertainty budgets for the NIST primary measurements of ^{18}F (August 2015) and ^{64}Cu (March 2016)**
4P-LS-BP-NA-GR-AC

Uncertainty contributions due to	**Evaluation method**	**Relative standard uncert. × 10^4**		**Comments**
		^{18}F	**^{64}Cu**	
Counting statistics	A	9	12	Counting statistics: Typical standard deviation of the mean for repeated activity determinations (N = 7 or 57 for ^{18}F; N = 45 to 102 for ^{64}Cu) on a single source on a single measurement run (averaged over 2 sources for ^{18}F ; average of 4 runs with 3 sources; one source measured on two occasions, with recovered activity consistent to 0.03 % for ^{64}Cu)
Between source variance	A	0.3	34	Standard deviation on the activities determined for multiple sources
Model uncertainty	B	28	32	Estimated by combining the typical difference on the activities recovered with a linear and a quadratic extrapolation (0.27 % for ^{18}F ; 0.32 % for ^{64}Cu) with the standard deviation of intercept values obtained with different gamma gates for ^{18}F or the standard deviation on the activity recovered from a linear extrapolation using domains of N = 7 to 12 efficiency points (0.06 %) for ^{64}Cu.
Mass determinations	B	5	5	
Live time	B	10	10	Estimated based on previous work
Background	B	3	10	Estimated by propagating the standard deviation of the mean for repeated (N = 10) measurements of the matched blank
Impurities	B	0	6	Based on HPGe measurements and estimates for LS efficiency
Half-life	B	8	2	From DDEP, $T_{1/2}(^{18}F)$ = 1.82890(23) h; $T_{1/2}(^{64}Cu)$ = 12.7004(20) h
β^+ branching ratio	B	20		From DDEP, 0.9686(19)
Relative combined standard uncertainty		38	51	