

Report of the NIST Radioactivity Group to CCRI Section II

Michael P. Unterweger
Leader, Radioactivity Group
Radiation and Biomolecular Physics Division
Physical Measurement Laboratory
National Institute of Standards and Technology
Gaithersburg, MD 20899-8460 USA

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This report is intended to be an overview of the activities of the Radioactivity Group at the National Institute of Standards and Technology (NIST) for the meeting of Section I (x and gamma rays, charged particles) of the Consultative Committee on Ionizing Radiation (CCRI), March 26-28, 2013. Since the last meeting of CCRI(II), a reorganization of the Ionizing Radiation Division has taken place, whereby it has been renamed the Radiation and Biomolecular Physics Division and is comprised of three groups: Dosimetry, Radioactivity, and Neutron Physics.

Technical highlights

- Calibration of epoxy based ^{133}Ba standard phantom sources for use in an international comparison for quantitative SPECT
The International Atomic Energy Agency (IAEA) recently initiated a Cooperative Research Project (CRP) entitled “Development of Quantitative Nuclear Medicine Imaging for Patient Specific Dosimetry” as part of a larger program aimed at enhancing the practice of nuclear medicine physics in its Member States. One of the early goals of the CRP is to assess the global state of the accuracy and consistency of Single Photon Emission Tomography (SPECT) image quantification, as evidenced by the performance of the institutions participating in the project during a series of comparison exercises.

Based on information provided by the participants regarding the type of instrumentation (i.e., activity calibrators and scanners) that they have available and the types of medical procedures that are performed in their centers, it was decided that ^{131}I should be used as the test radionuclide for the comparison because of its widespread use around amongst the Member States. As the quantity of interest is the accuracy with which the participants could determine the activity concentration of the radioactive sources using SPECT imaging, it was necessary for the activity content of the sources to be traceable to a single standard. The relatively short half-life ($T_{1/2}=8.0233(19)$ d) [1] of ^{131}I and the large distances between the participating laboratories made it logistically impossible to prepare and calibrate phantoms of ^{131}I and have them shipped to the participants with reasonable activity levels. For that reason, ^{133}Ba was chosen as a long-

lived surrogate because of its long half-life of 10.540(6) a [2] and the fact that the most abundant γ -ray in the decay of ^{133}Ba at 356 keV is similar in energy and emission probability to the most abundant γ -ray in the decay of ^{131}I at 364 keV. To minimize logistical problems associated with shipping liquid radioactive sources internationally, the test objects for the comparison were a set of 4 cylindrical phantom inserts, each containing a calibrated amount of ^{133}Ba in epoxy. The activity concentration in the three lowest volumes was to be about 200 kBq•g⁻¹ (denoted “high-level”) and that of the 23 mL sources was to be 50 kBq•g⁻¹ (denoted “low-level”).

- Primary standardization of radionuclides by anticoincidence counting

The standardization of radionuclides by primary methods is the foundation for all the standards and services provided by the NIST radioactivity group. These include: SRM's, special calibrations, and proficiency testing. The principle method of primary standardization at NIST is live-timed $4\pi\beta$ - γ anticoincidence counting (LTAC). Recently NIST researchers have extended this method to perform primary measurements on a variety of radionuclides that decay by alpha, beta and positron and electron-capture, most recently, ^{99}Tc , ^{131}I , ^{18}F , ^{237}Np and ^{124}I . Primary standards have been submitted to international comparisons and have been found to be in excellent agreement with other national metrology institutes. Furthermore, NIST researchers use these primary standards to calibrate their own secondary instruments, including ionization chambers and γ -ray spectrometers. This powerful tool was also recently used to make the definitive determination of the Liquid Scintillation (LS) wall-effect. Ongoing work includes improvement in accuracy by incorporating GEANT simulations into efficiency extrapolations and the inclusion of a digital electronics chain.
- FPGA-based Triple-to-Double Coincidence Ratio Liquid Scintillation Counting

The triple-to-double coincidence ratio (TDCR) method of liquid scintillation counting employs three detectors to facilitate the experimental determination of counting efficiencies so that activity can be measured independent of calibration standards. Together with the ^3H efficiency tracing liquid scintillation counting method and live-timed anticoincidence counting, TDCR counting is at the heart of many “primary” activity standardizations performed at NIST.

Implementation of the TDCR method at NIST has, until recently, relied upon the analog MAC3 logic unit first described by Bouchard and Cassette.¹ The unavailability of new and/or replacement units and the promise of increased flexibility in data acquisition parameters has spurred several laboratories to migrate to digital systems based on field programmable gate array (FPGA) technology. NIST has developed a

FPGA-based TDCR acquisition system using the LabView programming environment. Code for coincidence and livetime logic as well as for counting is compiled and uploaded to the FPGA, while code on the host computer provides the user interface, allowing for a wide range of acquisition parameters.

- **Micelle Effects in Liquid Scintillation Counting**

Commercially available scintillants (often referred to by manufacturers as “cocktails”) for liquid scintillation (LS) counting are complex concoctions of alcohols, phosphates, polymers, and salts in organic solvent. Various surfactants are used to suspend the aqueous fraction in the different cocktails, and it is in the resultant reverse micelles that the aqueous materials (typically metal ions or, in the case of tritium, water molecules) of interest in radionuclide metrology reside. While a rich and interesting field of research examines the specific physical chemistry of surface and interface interactions that determine micelle properties in a given environment, for any stable formulation, the radionuclide metrologist is concerned with one value: the micelle size.

This is because of the “micelle effect” on scintillation efficiency. When an electron is emitted from a radionuclide, it loses energy while traversing the aqueous material within a micelle. This energy is not deposited in the scintillation material, and so does not result in scintillation light. The distance that an electron must travel through an aqueous medium prior to interacting with the organic scintillator is therefore of interest when calculating theoretical scintillation efficiencies for a particular radionuclide in a particular scintillation cocktail. This problem can be particularly acute for low-energy Auger electron-emitting radionuclides.

- **Standardization of ^{244}Cm (SRM 4320b)**

Curium is a byproduct of plutonium production activities and results from the successive capture of neutrons by plutonium and americium, generally in nuclear reactors. In the environment it is found where releases from weapons production facilities have caused localized contamination. It is mainly used for research activities and monitoring of radiochemical procedures. A new standard solution of ^{244}Cm was developed and will be disseminated at NIST as SRM 4320b. The certified massic activity for ^{244}Cm in radioactive equilibrium with ^{240}Pu was obtained by $4\pi\alpha\beta$ liquid scintillation (LS) spectrometry with three commercial LS counters. Confirmatory measurements were performed by high-resolution HPGe gamma-ray spectrometry. The combined standard uncertainty ($k = 2$) on the standardization is 1.4 %. The certified value of the massic activity for SRM 4320b was in agreement with that for the previously issued SRM 4320a to within 1.0 %.

- **Primary Radioactivity Standardization of ^{237}Np (SRM 4341a)**

A new primary radioactivity standardization of ^{237}Np was performed. Neptunium-237 is produced as a long-lived waste product in nuclear reactors. Hence, accurate standardization is necessary for environmental monitoring of nuclear waste. The standardization of ^{237}Np by several primary methods was investigated. This was performed to support a new ^{237}Np transfer standard that was developed and which will be disseminated by the National Institute of Standards and Technology (NIST) as Standard Reference Material SRM 4341a. A EUROMET comparison hosted by NPL in 1998 identified ^{237}Np - ^{233}Pa equilibrium/stability issues. As a result of this study our master solution was diluted in steps, and stability tested at every step. Data suggested that the equilibrium was disturbed when aliquots were removed from the ampoule; hence sufficient time elapsed before standardization measurements were performed. The certified massic activity of SRM 4341a as obtained from the $4\pi\alpha\beta$ liquid scintillation based standardization could be directly compared to the results obtained from the weighted mean of 9 primary standardizations by 5 laboratories and performed in 1998-99 as part of the EUROMET ^{237}Np measurement comparison (-0.07 %). NIST confirmatory standardizations of the ^{237}Np massic activity for SRM 4341a were performed by live-timed anticoincidence (LTAC) $4\pi\beta(\text{LS}) - \gamma(\text{NaI})$ measurements and by high-resolution HPGe gamma-ray spectrometry (γ -spec) with a comparison difference of -0.13 % and 3.8 %, respectively. The uncertainty in the (γ -spec measurement was 6.5 % ($k = 1$). SRM 4341a was in agreement with the previous issue of ^{237}Np (SRM 4341), first disseminated in 1993, to within 0.03 %. The ^{237}Np SRM solution standards are contained in 5 mL flame-sealed borosilicate glass ampoules, and consist of (5.3196 ± 0.0003) g of a carrier-free nominal $2 \text{ mol}\cdot\text{L}^{-1}$ nitric acid solution, having a density of $(1.067 \pm 0.002) \text{ g}\cdot\text{mL}^{-1}$ at $16.3 \text{ }^\circ\text{C}$. The combined standard uncertainty ($k = 2$) on the standardization is 0.92 %.

- Standardization of ^{209}Po (SRM 4326a) and Evaluation of Half-life Discrepancy

A new primary standardization of ^{209}Po is underway to support the production and dissemination of a new series of carrier-free solution standards (SRM 4326a), as well as to provide a linkage to the previous SRM 4326. The ^{209}Po certified massic α -emission rate for SRM 4326a will be obtained with three commercial LS counters and with varying cocktail compositions. The new SRM, as the previous issue, will be prepared carrier-free in 2 mol/L HCl. Corrections for the electron capture branch to ^{209}Bi and for the 2-keV delayed isomeric state in ^{205}Pb will be made. Confirmatory measurements will be performed by α spectrometry with high resolution Si surface-barrier junction detectors. The linkage to the previous SRM 4326 standardization will obtain a third value for a 19-year decay curve, following those obtained from previous ^{209}Po standardizations performed in March 1994 and November 2005. The measurement procedures and analyses for the three determinations will be

as identical as possible. The new result may confirm or refute the serious 25 % half-life discrepancy that we identified in 2006. This work is a large and ambitious undertaking as reflected in the accompanying production and standardization schema.

- International comparison of Lu-177

There has been increasing interest during the past 10 years in the use of ^{177}Lu for radionuclide-based radiotherapy for certain types of cancers. Accurate administrations of drugs using this radionuclide require accurate standards against which instrumentation used in the clinics and radiopharmacies can be calibrated. Several new ^{177}Lu -based radiotherapy drugs are being investigated worldwide, which will cause an even greater need for such standards.

Lutetium-177 decays with three primary β branches ($E_{\beta\text{max}} = 176 \text{ keV}$, 385 keV , and 498 keV) and has two reasonably strong γ -rays at 113 keV and 208 keV , making it suitable for analysis using a variety of techniques, including coincidence counting. The only previous comparison of ^{177}Lu that has been carried out was a bilateral comparison (BIPM-R(II)-K1.Lu-177) conducted between the NIST and the PTB in 2000. In that case, both laboratories were able to submit ampoules to the SIR and report activity values based on liquid scintillation counting using the CIEMAT/NIST efficiency tracing method. The results indicated a difference of about 1.4 % in the International Reference System (SIR) equivalent activity. The short half-life of the ^{177}Lu did not allow for follow-up studies to be performed.

Since that time, several more NMIs have standardized this radionuclide. In order to establish a link between primary standards of β -emitters in the NMIs and the SIR, as well as to provide a means for laboratories to substantiate CMC claims for β - γ nuclides, a CCRI(II) Key Comparison of ^{177}Lu was carried out in the Spring of 2009 and the final results were published in 2012 [1].

A total of 12 laboratories took part in the comparison. One of the results was from a laboratory that was neither the national metrology institute (NMI) nor the designated institute (DI) for their country, so this was combined with that of the DI in their country to give a total of 11 values to go into the calculation of the Key Comparison Value (CRV).

The analysis of the set of results indicated that it was statistically inconsistent. Since the various tests that were applied to the data could not identify any single laboratory as being an outlier, an approach was taken that would allow all of the results to be used in the calculation of the CRV. To do this, it was assumed that the uncertainty in each laboratory's result contains both within-laboratory and (generally unobserved) between-laboratory sources of variability [2]. Applying the Maximum Likelihood

approach of Vangel and Rukhin [3] to the estimation of the consensus mean, a proposed CRV of $3.288(4) \text{ MBq}\cdot\text{g}^{-1}$ was calculated, where the quoted uncertainty corresponds to a standard ($k=1$) uncertainty interval that considers both within- and between- laboratory effects.

- Calibration of large-volume, solid ^{68}Ge phantom sources for monitoring PET scanner performance in clinical trials

The interpretation of quantitative imaging data obtained from Positron Emission Tomography (PET) studies requires an understanding of the measurement variability due to instrumental effects, especially in clinical trials that involve large numbers of patients being scanned in several sites with different types of scanners using a variety of acquisition and analysis techniques. Although the data from most PET studies are often used on a relative basis, the quality of the analysis will be greatly improved if the data can be normalized using a common reference standard that allows instrumental variability to be minimized. This requires long-lived PET phantoms to be available to all sites throughout the entire study and the activity content in the phantoms to be linked to a single standard.

Working in collaboration with a university medical center and a commercial source manufacturer, we have designed and calibrated two prototype large volume (30 cm length x 20 cm diameter, approximately 9 L) cylindrical phantom sources containing ^{68}Ge in epoxy as a surrogate for ^{18}F that can be used to accomplish these tasks. The design is similar to the phantoms used clinically with ^{18}F to calibrate the PET scanners and are the first ones having a calibrated value for the amount of ^{68}Ge in the phantom that is directly traceable to a national standard for that radionuclide. Because of their large physical volume, direct calibration measurements on the phantoms were deemed unlikely to satisfy the requirement of having a combined uncertainty on the ^{68}Ge activity concentration of about 1 %. Therefore, a sampling procedure was adopted in which samples of the epoxy containing ^{68}Ge were taken during the phantom preparation process and dispensed into a standardized geometry for calibration. The epoxy sources were measured on several HPGe systems that been calibrated for this specific geometry using a previously standardized ^{68}Ge solution. Corrections were made for possible differences in attenuation and scattering arising from the differences in composition and density between the epoxy and solution sources. From the known mass of the epoxy in each of the samples and these activity measurements, the activity concentration of the epoxy in the phantoms was determined with a combined standard uncertainty of less than 1 %. The relative difference in activity concentration between the two prototypes, as well as the measured variability in the activity concentration in each phantom (uniformity), was confirmed by scanning the phantoms in the NIST PET-CT scanner.

Using this new procedure, it is now possible to calibrate nearly any type of epoxy phantom for ^{68}Ge activity concentration against a national standard. Because the uncertainty on the activity concentration value for these phantoms is well below the typical uncertainties encountered in the PET-CT scanning process, systematic investigations of the uncertainty components associated with PET imaging using these sources are now possible.

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Comparisons Done in 2011-2013

- CCRI(II)-S8 bilberries Report in progress, Draft A
- CCRI(II)-K2.Tc-99 comparison In progress

Future Comparisons

- CCRI(II)-S10 LASCE (Measurement of source emission rate for the calibration of surface contamination monitors) 2011 – 2012 In progress

- CCRI(II)- K2.Lu- 177 (Activity concentration of the same Lu-177 solution) 2009
Report in progress, Draft B

Facility upgrades

- Hoods in all laboratories were all upgraded in 2012
- Mass spectrometer ordered and being installed in 2013
- Automated multi-sample ionization chamber for radioactivity standards
NIST radioactivity standards for gamma-ray emitting radionuclides are maintained as calibration factors for an automated ionization chamber. This instrument has been developed at NIST to measure up to 100 samples with programmable sample queuing, sample handling and measurement parameters while maintaining the high precision and reproducibility of a similar manual instrument that has been used for over 30 years. Routine use of this new instrument results in reduced radiation exposure to operators, expedites the standards-transfer process and improves quality assurance. NIST has recently established calibration factors for the instrument for ^{131}I , ^{18}F , ^{124}I and ^{201}Tl , using NIST primary standardizations.