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Proficiency tests in the determination of activity of radionuclides in radiopharmaceutical products measured by nuclear medicine services in 8 years of comparison programmes in Brazil

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Abstract

Proficiency tests were applied to assess the performance of 74 nuclear medicine services in activity measurements of ^{131}I, ^{123}I, ^{99}Tc^{m}, ^{67}Ga and ^{201}Tl. These tests produced 913 data sets from comparison programmes promoted by the National Laboratory for Ionizing Radiation Metrology (LNMRI) from 1999 to 2006.

The data were evaluated against acceptance criteria for accuracy and precision and assigned as *Acceptable* or *Not acceptable* accordingly. In addition, three other statistical parameters were used as complementary information for performance evaluation which related to normative requirements and to radionuclide calibrators.

The results have shown a necessity to improve quality control procedures and unsatisfactory performances of radionuclide calibrators, which incorporate Geiger–Müller detectors.

Keywords: Intercomparison; Proficiency test; Nuclear medicine services; Radionuclide calibrators

1. Introduction

The metrology of radionuclide activity is an important feature of life sciences. Due to the recognition of the implementation of Quality Assurance (QA) programmes to guarantee the accuracy, precision and consistency of the measurements, it is easy to understand their application in the nuclear medicine field (Debertin and Schrader, 1992; Iwahara et al., 2001; Joseph et al., 2003; Oropesa et al., 2003).

The availability of standards with metrological traceability to calibrate instruments and to verify the performance of activity measurement enables the establishment of a quality control programme in the use of radiopharmaceutical products.

In nuclear medicine services (NMSs), many types of radioactive substances are used, for diagnostic and therapy routines. The equipment used to measure the activity of the radionuclide is the radionuclide calibrator. This instrument is composed of an ionization chamber (or Geiger–Müller detector) coupled to an electrometer with a direct display reading in activity units.

The procedures related to activity measurements in NMSs are regulated by norms or recommendations

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established by authorities that detail the legal responsibility in these fields. These regulations apply to the radiopharmaceutical supplier of radionuclide calibrators and to the users in NMSs. The regulations need to specify the necessary accuracy in the measurement of the activity and the activity of radiopharmaceutical products administered to the patient and the need to make the data available to the regulatory authority.

The International Atomic Energy Agency (IAEA) and European Pharmacopoeia recommend a maximum deviation of $\pm 5\%$ when it refers to accuracy of measurement in radionuclide calibrators (IAEA, 2006; European Pharmacopoeia, 2001). In Brazil, the required accuracy for diagnostic purposes is established in the norm NN.3.05 of the National Commission on Nuclear Energy (CNEN) that recommends percentage deviations up to $\pm 10\%$ (CNEN, 1996).

The activity administered to the patient should be as close as possible to that prescribed by the physician. If it is smaller, the patient may probably need an additional administration to obtain the desired clinical result (for example, good image for diagnosis) and this results in an unwanted dose. If the activity is larger, the patient will equally be receiving an unnecessary dose of ionizing radiation.

With the objective of evaluating the quality of routine measurements of activity in the NMSs, the LNMRI of the Radiation Protection and Dosimetry Institute (IRD) of CNEN, has coordinated comparison programmes of activity measurements of radiopharmaceutical products used in nuclear medicine practices. The participation in the comparison programme is voluntary and open to all NMSs of hospitals and clinics in the country.

According to CNEN in 2006, there were 247 NMSs distributed in Brazil. This number is variable, because many services are receiving new authorizations to operate and others are finishing their activities. In the period from 1999 to 2006, 74 NMSs localized in the state of Rio de Janeiro, Porto Alegre City and Center-West region, using a National Metrology Network coordinated by LNMRI, have participated in the comparison exercises. In these comparisons, the radionuclides $^{99}Tc^{m}$, ^{123}I, ^{131}I, ^{67}Ga and ^{201}Tl were used (dos Santos et al., 2006).

In this work, with the purpose of homogenizing the evaluation procedure of the comparisons, the recommendations of ISO-GUIDE 43, IAEA and BIPM (IAEA, 2006; ISO/IEC Guide 43-1, 1997) were applied.

The performance evaluation was made also using the value of the ratio of the mean value of five measurements realized by the participant NMSs, and the value obtained by LNMRI. The LNMRI value was used as the reference value, to be compared with the normative requirement (CNEN, 1996).

The two principal evaluation procedures looked at the accuracy and the precision of the results. Both of these procedures include the total combined uncertainty associated with the measurement of the participant NMS as well as the uncertainty associated with the reference value. In addition, three other statistical criteria namely: *Z-score*, *Relative bias* and *Ratio* ($Value_{NMS}/Value_{LNMRI}$) were obtained as complementary information.

In order for the overall NMS result to be assigned as *Acceptable*, all of the individual criteria (with the exception of the *Ratio Value*) have to be acceptable.

2. Methodology

The proficiency test performance evaluation was applied to each comparison run. For each radionuclide, the reference value and its associated uncertainty were established by LNMRI using an IG12 ionization chamber that was calibrated with standard sources that, in turn, were standardized using the primary standardization systems of LNMRI.

The final result of the performance evaluation was defined by the combined results of *Precision*, *Accuracy*, *Z-score and Relative bias* (ISO, 1997).

Using this approach, this evaluation was applied to 913 results obtained in the comparison programmes of radionuclide activity measurements of radiopharmaceutical products in the period from 1999 to 2006. With the aim of comparing the performance of NMSs with the criteria of proficiency test related to the requirement of the Brazilian norm, the value of *Ratio* ($Value_{NMS}/Value_{LNMRI}$) was also used.

(a) Accuracy:

The accuracy was evaluated using the U_{Score} value,

$$U_{Score} = \left| \frac{Value_{LNMRI} - Value_{NMS}}{k \times \sqrt{u_{LNMRI}^2 + u_{NMS}^2}} \right|$$

where $Value_{LNMRI}$, LNMRI reference value established for each radionuclide; $Value_{NMS}$, mean value of five NMS activity measurements for each radionuclide; u_{LNMRI}, combined standard uncertainty ($k = 1$) of the reference value; u_{NMS}, total standard uncertainty ($k = 1$) of NMS measurement; k, coverage factor; in this work was used $k = 1.96$ for confidence level of 95%.

The evaluation criterion was

$|U_{Test}| \leqslant 1$ *Acceptable*.

(b) Precision:

$$P = \sqrt{\left(\frac{s_{LNMRI}}{Value_{LNMRI}}\right)^2 + \left(\frac{s_{NMS}}{Value_{NMS}}\right)^2} \times 100\%$$

where s, standard deviation of measurements.

The acceptance criterion was $P \leqslant 5\%$ (IAEA, 2006).

(c) Relative bias:

$$Relative\ bias = \frac{Value_{NMS} - Value_{LNMRI}}{Value_{LNMRI}} \times 100\%.$$

The acceptance criterion was the *Relative bias* $< \pm 10\%$.