Protocol for the CCRI(II)-K2.Ge-68 comparison
Updated 28 October 2014

1. Introduction

There has been increasing interest in the use of ^{68}Ge + ^{68}Ga as a surrogate for ^{18}F in quantitative imaging, as well as increasing interest in the use of ^{68}Ga 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.

Germanium-68 decays with a half-life of 270.95(26) days by pure electron capture to the ground state of ^{68}Ga. Gallium-68 decays by both positron emission and by electron capture, mainly to the ground state of ^{68}Zn with a half-life of 67.83(20) minutes. Additionally there is decay to a 1077 keV excited state with a probability of about 3 % and decay to several higher excited states with a combined probability less than 0.4 %. This decay scheme makes it suitable for analysis using a variety of techniques, including liquid-scintillation counting and coincidence counting.

To date, there are no reported submissions to the SIR of ^{68}Ge. Three NMIs have reported standardizing this radionuclide. Several more have reported standardizing the daughter radionuclide alone. In order to provide a means for laboratories to substantiate CMC claims for this nuclide, a Key Comparison of ^{68}Ge is proposed. This proposal is initiated as an Action Item arising from a meeting of the Life Sciences Working Group (LSWG) of the International Committee on Radionuclide Metrology (ICRM).

IMPORTANT SAFETY NOTE: The carrier solution composition has been carefully chosen, based on Mirzadeh and Lambrecht, 1995, to avoid the potential volatility of germanium from solution. Germanium will volatilize if the solution is taken to dryness. This includes remainder solutions in open containers. It is suggested that work be performed in radiological fume hood and closed containers are used for all storage of waste materials. Participants are referred to Grigorescu, et al., 2004 for experience in production of dry sources.

2. Comparison Protocol

Pilot Institute: National Institute of Standards and Technology (NIST), United States

List of Participants:

ANSTO, Australia
BARC, India
CIEMAT, Spain
IFIN-HH, Romania
INER, Taiwan
IRA, Switzerland
IRMM, International
KRISS, Republic of Korea
LNE-LNHB, France
LNMRI/IRD, Brazil
NIM, China
NMIJ, Japan
NIST, United States
NPL, United Kingdom
POLATOM, Poland
PTB, Germany
SMU, Slovakia
TAEK, Turkey

Comparison Nuclide Solution: ^{68}Ge + ^{68}Ga chloride containing nominally 5 MBq at time of shipment to be dispatched by NIST

Container: NIST-style ampoule supplied by NIST, to be transferred by each participant into BIPM ampoules for submission to the SIR

Mass: approximately 5 g

Chemistry: in carrier containing 0.5 mol·L^{-1} HCl and approx. 65 μg/g of solution each nonactive Ge^{+4} and Ga^{+3} ions

Recommended Nuclear Data: BIPM Monographie BIPM-5, Vol 7, pp 33-45 (2013).

2.1 Measurand: **The measurand for this exercise is activity of ^{68}Ge per unit mass.**

2.2 All participants are encouraged to send an ampoule containing 3.6 g of solution to the BIPM for measurement in the SIR and to use the usual SIR reporting form. For instruction, see: http://www.bipm.org/en/scientific/ionizing/radionuclides/sir/participation.html.

2.3 Schedule

Starting date: The starting date for this programme is 20 October, 2014.

Distribution: The solutions were prepared on 7 August 2014 and distributed to participants during October 2014.

Deadline for submission of all appropriate shipping, customs, and special handling information will be 30 April 2014 (5 weeks prior to anticipated shipment date).

Those laboratories submitting sources to the BIPM are requested to submit a Pro Forma invoice to the BIPM prior to 30 April 2014, an example of which is attached to this protocol.

Based on the sources being distributed in Late-October, the following schedule for reporting is proposed:

Reporting opens: NIST will announce the opening of the reporting period after NIST results are submitted to the BIPM.

Reporting deadline: 16 January 2015

Draft A sent to participants: 6 March 2015

Draft A acceptance deadline: 8 May 2015

Draft B sent to participants: 19 June 2015

Draft B acceptance deadline: 17 July 2015

Participants shall report their results at a comparison **reference time** of **1200 UTC 14 November 2014**.

2.4 NIST shall be responsible for maintaining up-to-date key comparison status reports and shall transmit them to the executive secretary of CCRI(II).

2.5 Each participating institution is responsible for its own costs associated with the measurements, as well those for transportation and customs and any damage that may occur within its country. The costs associated with organization of the comparison, preparing, calibrating, and shipping the ^{68}Ge comparison solutions will be borne by NIST.

2.6 All results, method of standardisation, associated uncertainties, and any additional requested information shall be transmitted to NIST using the reporting forms to be provided.

2.7 Participants must provide a list and evaluation of the principal components of the uncertainty budget based on the Guide to the Expression of Uncertainty in Measurement, published by ISO (http://www.bipm.org/en/publications/guides/gum.html). In addition to the principal

components of the uncertainty, common to all of the participants, individual institutes must add any other components they consider appropriate. Uncertainties are evaluated at a level of one standard uncertainty and information must be given on the number of effective degrees of freedom, required for a proper estimate of the level of confidence, where this is appropriate.

2.8 Transport of the ^{68}Ge ampoules to the participants will be arranged by NIST using their normal radioactive shipment arrangements. Immediately after receipt, the participating institute shall check for any damage to the samples and report this to NIST.

2.9 If delays occur, NIST shall inform the participants and revise the schedule, if necessary.

3. Preparation of the report on the comparison

NIST is responsible for the preparation of a report on the comparison. The report passes through a number of stages before publication, and these are referred to here as drafts A and B.

3.1 During the comparison, as the results are received by NIST, they are kept confidential by NIST until all the participants have completed their measurements and all the results have been received, or until the deadline for receipt of results has passed.

3.2 A result from a participant is not considered complete without an associated uncertainty, and is not included in the draft report unless it is accompanied by an uncertainty supported by a complete uncertainty budget. Uncertainties are drawn up following the guidance given in the technical protocol.

3.3 If, on examination of the complete set of results, NIST finds results that appear to be anomalous, the corresponding institutes are invited to check their results for numerical errors but without being informed as to the magnitude or sign of the apparent anomaly. If no numerical error is found the result stands and the complete set of results is sent to all participants.

3.4 The first draft, draft A, is prepared as soon as all the results have been received from and, if necessary, confirmed by the participants. It includes the results, uncertainties, standardization methods and experimental details transmitted by the participants, identified by name.

3.5 Draft A of the report is sent as soon as possible after completion of the comparison to all the participants for comment, with a reasonable deadline for replies. The date at which this draft is sent to the participants is taken to be the end date for the comparison and is subsequently referred to as such.

3.6 If any controversial or contradictory comments are received by NIST, they will be circulated to all participants and discussion continues until a consensus is reached.

3.7 Draft A is considered as confidential to the participants. Copies are not given to non-participants, and graphs or other parts of the draft are not used in oral presentations at an external Conference without the specific agreement of all the participants. (The results may be the subject of an internal report if they are shown in relative terms and the name of participants hidden. At this stage, a participant may publish experimental techniques of special interest or new developments

of a measurement method made in the frame of the comparison, as long as no information or comments are made about the comparison results.)

3.8 Note that once all participants have been informed of the results, individual values and uncertainties may be changed or removed, or the complete comparison abandoned, only with the agreement of all participants and on the basis of a clear failure of the comparison artifact or some other phenomenon that renders the comparison or part of it invalid.

3.9 An institute that considers its result unrepresentative of its standards may submit another solution to the SIR based on a new primary measurement. The subsequent comparison is considered as a new and distinct comparison.

3.10 On receipt of final comments from participants, the second draft, draft B, is prepared by the BIPM incorporating the agreed comments on the draft A, and also the SIR results.

3.11 As the comparison will be linked to the SIR, the KCRV (in terms of SIR Equivalent Activity) will be determined by the BIPM and the Appendix will be produced by the KCWG, including the comparison results in the SIR mother file, KCRV file and equivalence files.

3.12 The draft B is circulated through the participants. Once agreed, draft B is not considered confidential and may be the subject of a publication, with the exception of the Appendix containing proposals for the reference value and degrees of equivalence.

3.13 Draft B will be sent to the CCRI(II) for review and approval.

3.14 In the event that there is disagreement concerning the results or the interpretation of the results of a key comparison, and the disagreement cannot be resolved by the participants, by the key comparison working group or by the Consultative Committee, the matter is referred to the CIPM for decision.

4. References

S. Mirzadeh and R.M. Lambrecht, Radiochemistry of Germanium, *J. of Radioanal. Nucl. Chem.* **202**, 7-102 (1996).

E. L. Grigorescu, C. D. Negut, A. Luca, A. C. Razdolescu, and M. Tanase, Standardization of ^{68}(Ge + Ga), *Appl. Radiat. Isot*. **60**, 429-432 (2004).

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