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Peter MacCallum Cancer Centre onsite Terbium 161 gamma measurements with portable HPGe detector

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Introduction

In May 2022, two representatives (Michelle Thomas and Callum Watson) from the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) Monitoring and Emergency Response Section attended a request to assist in the measurement of Terbium 161 (^{161}Tb) for a new clinical trial at the Peter MacCallum Cancer Centre (PMCC) on Grattan Street, Melbourne, Victoria.

The dose calibration and measurement devices used in hospitals are not currently set up to measure ^{161}Tb, as it is a relatively new isotope in nuclear medicine (Juget et al., 2022). As part of their method development, PMCC staff have set a dedicated dose calibrator and measuring device capable of measuring ^{161}Tb, but wanted an independent assessment to confirm their activity measurements for quality assurance purposes.

Contents

Acknowledgements

The authors wish to acknowledge the support from staff at the PMCC – Brittany Emmerson, Michael Gilhen and Lachlan McIntosh.

Acknowledgement of Country

The Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) respectfully acknowledges Aboriginal and Torres Strait Islander peoples, communities and their rich cultures. We pay respects to all Elders past and present. We acknowledge Aboriginal and Torres Strait Islander peoples as Australia’s First Peoples and the Traditional Owners and Custodians of the lands and waters where we live and work.

We also recognise and value the ongoing contribution of Aboriginal and Torres Strait Islander peoples and communities to Australian life and how this enriches us. We embrace the spirit of reconciliation, working towards the equality of outcomes and ensuring an equal voice.

Executive Summary

On Tuesday 24 May 2022, ARPANSA – on behalf of PMCC staff – undertook a series of gamma measurement activities of a ^{161}Tb solution in different vial and syringe geometries. These measurements were taken using a Falcon 5000 high resolution portable radionuclide identifier with a high purity germanium (HPGe) detector to:

- generate a high-resolution gamma spectrum for ^{161}Tb
- provide independent assessment of the amount of radioactivity of the ^{161}Tb to PMCC staff
- understand the impacts of sample geometry in radioactivity measurement.

A high-resolution gamma spectrum for ^{161}Tb and background spectrum was obtained on the Falcon 5000 and is presented in this report.

Results from the Falcon 5000 show good agreement (within 95% confidence interval) with PMCC expected activities of the ^{161}Tb solutions for FILL-EASE™ sterile vacuum vials in volumes ranging from approximately 0.5 mL to 6 mL. Activities of ^{161}Tb solution in syringe geometries show variations of 31.8% – 33.8% between results measured by PMCC staff, and the measurements obtained on the Falcon 5000 with revised in situ object counting system (ISOCs) geometries. These results may warrant application of a syringe correction factor to activity measurement readings on the PMCC dose calibration device to account for differences in geometry and measurement vessel composition.

Objective

As agreed with PMCC Radiation Safety officer Michael Gilhen, ARPANSA staff undertook the following activities and subtasks:

- To generate a high-resolution gamma spectrum for ^{161}Tb.
  - Provide Gamma spectrum in physical (this report) and electronic formats.
- To provide an independent assessment of the amount of radioactivity of the ^{161}Tb to PMCC staff.
  - Determine and generate suitable ISOCS container geometries of syringe and vial for efficiency calibration purposes.
  - Addition of ^{161}Tb nuclide data to Gennie 2000 library.
  - Conduct in situ measurement of varying activities of ^{161}Tb in geometries expected to be used working with ^{161}Tb.
  - Provide measurement data to PMCC staff.
- To understand the impacts of sample geometry in radioactivity measurement.
  - Provide a summary of the ARPANSA measurement and geometry data.

1. Gamma spectrometry measurement methodology

1.1 ISOCS geometries

Preliminary geometries of the vial and syringe were generated prior to attending the PMCC based on data supplied by PMCC staff. This allowed for preliminary results to be given to PMCC staff in real time.

Further refinement of the geometry models was conducted by ARPANSA staff after the site visit, based on sample vessel measurements and manufacture/product information. This information is presented in Appendix A.

1.2 Emission intensity measurements of ^{161}Tb key lines

Thirty-eight emission lines are listed for ^{161}Tb in the Nucléide – Lara Library for gamma and alpha emissions (Nucléide – Lara, 2022a). The 10 most intense lines are listed in Table 1 in order of decreasing intensity. For an emission line to be a suitable candidate for gamma spectrometry activity determinations, it must have the following characteristics:

1. Suitable emission intensity to allow for integration.
2. Little interference from other emission energies expected to be in the spectrum, such as from true coincidence summing, or from contaminating nuclides or spectrum artifacts also present with similar emission energies.

All the high intensity lines for ^{161}Tb are in a problematic region of the spectrum prone to electronic noise effects and low energy X-rays.

Potential key gamma emission lines which were initially considered as being suitable for measurement purposes are highlighted in yellow in Table 1 below and were added to a standard Genie 2000 nuclide library to enable identification and quantification of ^{161}Tb activity.

High intensity lines not considered for nuclide identification and activity calculation are as follows.

- The 7.2 Kiloelectron volts (keV) (22.0%) line is in a very low energy region of the spectrum and likely to have interferences from the Compton edge and other spectral artifacts.
- The 45.91 (11.2%) and 45.21 (6.28%) keV X-rays are very close together in energy and likely to be unresolvable.
- The 52.19 KeV (3.60%) peak is likely to be interfered by random summing of the 25.65136 (23.2%) keV gamma rays (25.65136 +25.65136 = 51.3 keV).

Table 1. The top ten ^{161}Tb Emissions sorted by decreasing intensity (Nucléide – Lara, 2022a)

Energy (keV)	Intensity (%)	Type
25.65136 (3)	***23.2 (15)***	***γ***
7.24245 (-)	*22.0 (5)*	X_L
48.91533 (5)	***17.0 (9)***	***γ***
45.999 (-)	*11.2 (5)*	$X_{K\alpha 1}$
74.56669 (6)	***10.2 (5)***	***γ***
45.2083 (-)	*6.28 (29)*	$X_{K\alpha 2}$
52.191 (-)	3.60 (17)	$X_{K'\beta 1}$
57.1917 (3)	***1.78 (10)***	***γ***
53.6353 (-)	0.94 (5)	$X_{K'\beta 2}$
87.941 (4)	0.183 (10)	γ

1.3 In situ gamma measurements

1.3.1 Configuration and set up of the Falcon 5000

Measurement of ^{161}Tb samples was conducted in a room deemed, by PMCC staff, to be away from any lutetium (^{177}Lu) usage. If present, lutetium could contribute to high background in the low gamma background in the region around the ^{161}Tb key lines (specifically the 57.19 and 74.56 keV lines), due to its 71.62 keV gamma emission and 55.79 keV X-ray (Nucléide – Lara, 2022b). Figure 1 shows positioning of the Falcon 5000 with a clear path between the face of the detector end cap to the ^{161}Tb source (indicated by a plastic cup).

Figure 1: In situ set up of the Falcon 5000 for gamma measurement.

1.3.2 Background measurement

A background spectrum was the first measurement taken to ensure the environment was suitable for ^{161}Tb measurements. Screenshots of the spectrum in Figures 2 and 3 show some peaks at 73.2, 75.4 (and at 85.5 and 87.7 keV), which are close to the ^{161}Tb 74.6 keV emission peak. These are characteristic spectrum artifacts due to X-rays produced via the photoelectric effects from lead shielding (NRC, 2012), which is likely to be in heavy use throughout the department.

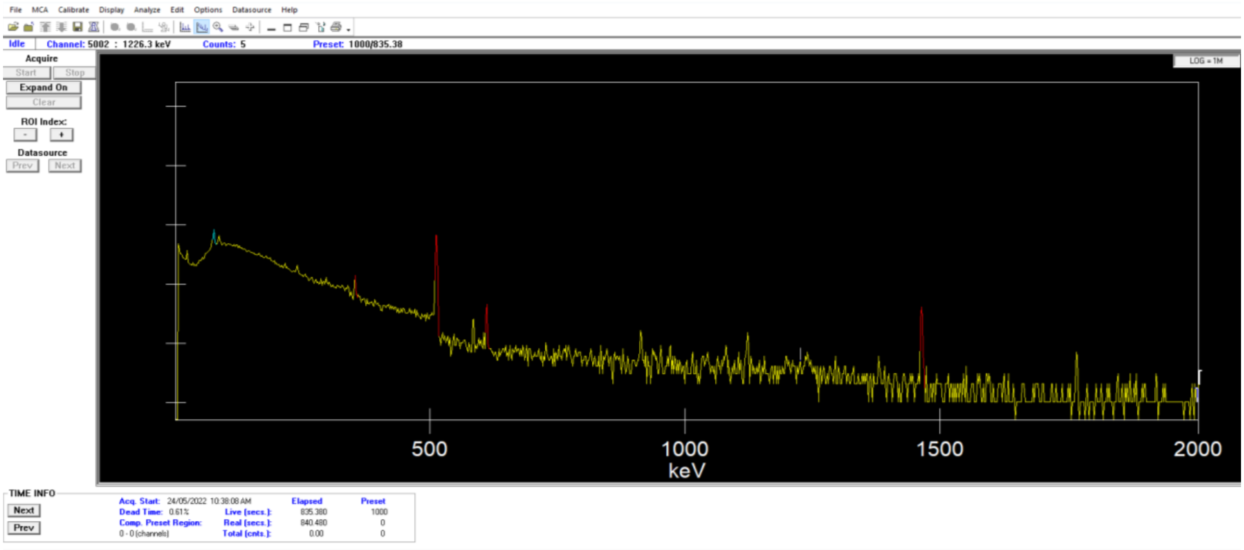

Figure 2: Screenshot of the background spectrum showing full energy range.

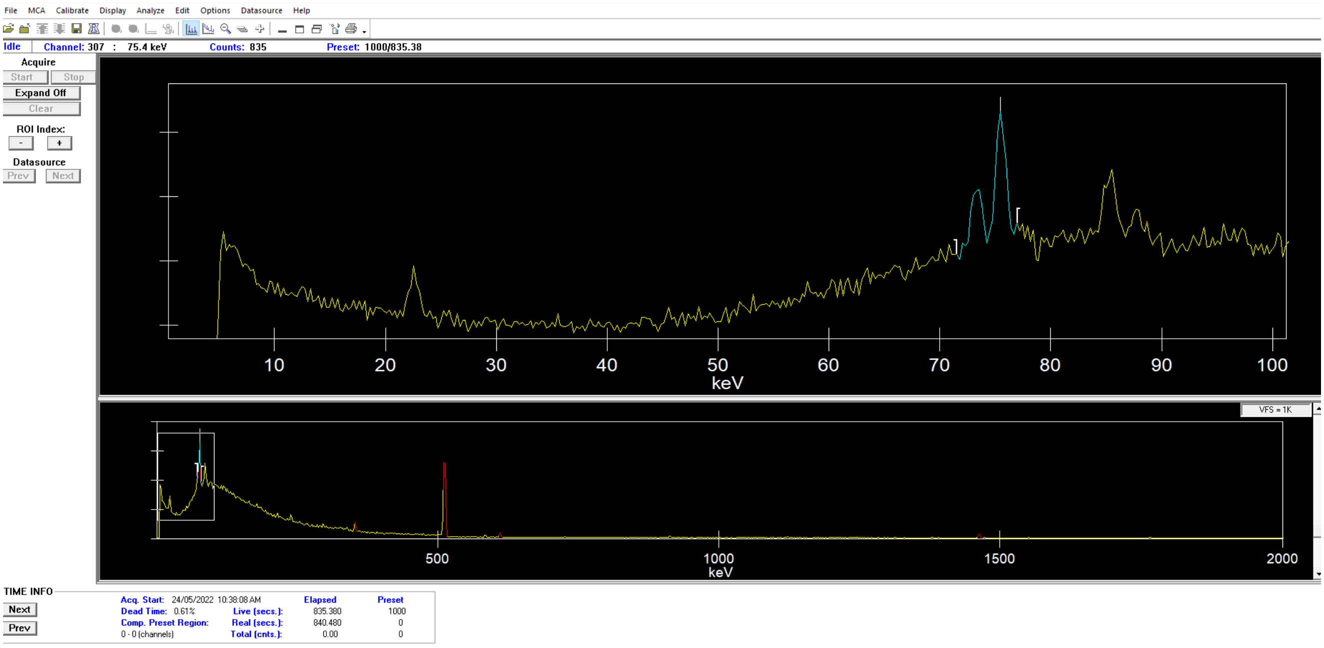

Figure 3: Close up view of the background file low energy region (below 100keV), showing the characteristic X-rays peaks at 73.2, 75.4, 85.5 and 87.7 keV due to the photoelectric effect of lead shielding.

1.3.3 ^{161}Tb solution measurements in various geometries

Six different measurements of varying amounts of ^{161}Tb solution in different vial and syringe geometries were taken by ARPANSA staff, each for 500 seconds and at a set distance from the Falcon 5000 endcap of 2,100 cm. Preliminary results are tabulated in Table 2 in Section 2.4 Results (below).

Geometry files were then refined by ARPANSA staff after this date with additional sample vessel information (refer to Appendix A) and reported in Table 3. Reported activities in this table are background corrected and corrected to the PMCC dose calibrator time and dates.

1.4 Results

PMCC staff tabulated sample details such as pre and post vessel weight and dose calibration measurements. Due to preconstructed preliminary geometries in the Genie 2000 software, ARPANSA staff were able to give estimates of the activity in the ^{161}Tb samples to PMCC staff at the time. This activity reading was based on a roughly calculated average for three of the chosen ^{161}Tb lines (48.92, 57.2 and 74.6 keV) without background spectrum subtraction. The 25.6 keV line wasn't included, as it showed substantially lower activity than the other 3 lines, likely due to random summing effects resulting in the peak at 51 keV.

Physical measurements were made on the vials and syringes to construct accurate models in the Gennie ISOCS software. Composition of the vessel material (borosilicate glass, polycarbonate, and polyethylene) was determined from manufacture supplied or issued information and is detailed in Appendix A. Results using these revised geometries with 95% confidence interval are detailed in Table 3. Screenshots of the spectra for vessels A to F can be found in Appendix B.

Table 2. PMCC ^{161}Tb sample details and dose calibrator readings. The initial Falcon 5000 gamma measurements for the samples given to the PMCC staff on the day are detailed in the last 3 columns.

PMCC 161Tb sample details						PMCC dose calibration			Initial Falcon 5000 gamma measurement		
Vessel ID	**Vessel geometry**	**Vessel Pre-weight (g)**	**Vessel Post Weight (g)**	**Weight of ^{161}Tb-PSMA (g or mL)**	**Dose Cal MBq**	**Date**	**Time**	**Dose Cal MBq**	**Date**	**Time**	**Preliminary Activity MBq**
A	16 mL vial	*	*	6 mL	42.5	24/05/2022	10:42	**42.5**	24/05/2022	*	**38 - 45**
B	12 mL vial	11.4765	12.0038	0.5273	28.3	24/05/2022	11:44	**28.3**	24/05/2022	12:00	**30**
C	16 mL vial	15.2603	15.7831	0.5228	26.7	24/05/2022	11:46	**26.7**	24/05/2022	12:14	**27**
D	23 mL vial	18.9418	19.417	0.4752	23.4	24/05/2022	11:45	**23.4**	24/05/2022	*	**22-23**
E	5 mL syringe	4.6305	5.1381	0.5076	34.3	24/05/2022	11:52	**34.3**	24/05/2022	*	**30-37**
F	1 mL syringe	7.36**	7.8765	0.5165	35.3	24/05/2022	11:54	**35.3**	24/05/2022	13:00	**34.8**

* Not recorded

** pre weight is an estimate

Table 3: Revised ISOCS modelled Falcon 5000 Gamma measurements, PMCC dose calibrator measurement activities, and percent difference calculations between the Falcon 5000 and PMCC activity shown for comparison purposes.

PMCC ^{161}Tb sample details				PMCC dose calibrator Activity per vessel	Revised ISOCS **Falcon 5000** Activity per Vessel		% Difference in Activities
Vessel ID	**Vessel geometry**	**Date**	**Time**	**MBq**	**MBq**	**Uncertainty (k=2) MBq**	
A	16 mL vial	24/05/2022	10:42	42.5	38.4	9.8	-10.2
B	12 mL vial	24/05/2022	11:44	28.3	26.9	6.8	-5.3
C	16 mL vial	24/05/2022	11:46	26.7	24.5	6.2	-8.4
D	23 mL vial	24/05/2022	11:45	23.4	20.9	5.3	-11.6
E	5 mL syringe	24/05/2022	11:52	34.3	24.9	6.3	**-31.8**
F	1 mL syringe	24/05/2022	11:54	35.3	25.1	6.3	**-33.8**

1.4.1 Discussion

PMCC measured dose calibrator activities for the vial geometries (sample IDs A to D) are within the uncertainties of the revised ISOCS modelled Falcon 5000 gamma measurements, with less than 12% difference between the 2 measurements (refer to Table 3).

The syringe geometries (vessel IDs E and F) for the PMCC dose calibrator activities show higher readings when compared to the Falcon 5000. This could indicate that a syringe correction factor may need to be applied to the PMCC dose calibrator when measuring ^{161}Tb solutions in syringe geometries. From the results in Table 3, there is 31.8% – 33.8% difference between the Falcon 5000 and PMCC dose calibrator activity readings for the syringe geometries.

This variation between vial and syringe readings can be seen if activity concentration per unit (i.e. MBq/µg) is calculated (refer to Table 4). Vessel IDs B to F all contain a similar amount of liquid (refer to third column in Table 4), yet the activity concentration per µg or µL varies depending on whether it was in a vial or a syringe for the PMCC measurements. For the PMCC measurement results, the vial geometries in vessel IDs B to D have an average activity result of 0.051 MBq/µg, while the syringe geometries (vessel IDs E and F) have a higher average activity concentration of 0.068 (a difference 28% between the 2 geometry types). Within the revised ISOCS Falcon 5000 measurements results, there is a difference of 3.4% between vial and syringe vessel types, indicating that the revised ISOCS geometry model was adequately accounting for attenuation differences in the different vessel materials.

Vessel ID A has a very different activity concentration (not shown in Table 4) compared to the other vial geometries. This may be because it has a different activity concentration (i.e., there is 42.5 MBq in approximately 6 mL), or it could be due to geometry effects, as the fill height of 6 mL in a 6 mL vial is different to the 0.5 mL fill height in a vial. To rule this out, a 0.5 mL ^{161}Tb sample in a vial could be measured, then diluted to 6 mL and remeasured. The activity reading of the 2 measurements will be the same if the fill height in the vial has no effect on ^{161}Tb gamma attenuation.

Efficiency values for key lines used in the activity calculation for the revised ISOCS Falcon 5000 geometries are presented in Table 5. If there the average efficiency for all lines for vessel type is taken, there is 20.73% difference between the 2 types.

Table 4: Average activity concentration calculations and percent difference calculations for PMCC dose calibrator and revised ISOCS Falcon 5000 measurements.

			PMCC dose calibrator measurements			Revised ISOCS Falcon 5000 measurements		
Vessel ID	**Vessel**	**Weight or volume of ^{161}Tb-PSMA (µL or µg)***	**Total Activity Dose Calibrator (MBq/vial)**	**Activity concentration (MBq/µl or MBq/µg)**	**Average activity concentration for vessel type**	**Total activity Falcon 5000 (MBq/vial)**	**Activity concentration (MBq/µl or MBq/µg)**	**Average activity concentration for vessel type**
B	12 mL vial	527.3	28.3	0.054	0.051	26.9	0.051	0.047
C	16 mL vial	522.8	26.7	0.051		24.5	0.047	
D	23 mL vial	475.2	23.4	0.049		20.9	0.044	
E	5 mL syringe	507.6	34.3	0.068	0.068	24.9	0.049	0.049
F	1 mL syringe	516.5	35.3	0.068		25.1	0.049	
* A density of 1.0 is assumed			Average of vial and syringes:		0.060	Average of vial and syringes:		0.048
			Absolute difference between average of vial (B to D) and syringe (E to F) vessel types:		0.017	Absolute difference between average of vial (B to D) and syringe (E to F) vessel types		0.002
			% difference between average of vial (B to D) and syringe (E to F) vessel types:		27.9%	% difference between average of vial (B to D) and syringe (E to F) vessel types		3.4%

Table 5: Revised ISOCS Falcon efficiency values showing calculation for percent difference between the vial and syringe vessel types.

		Revised ISOCS Falcon 5000 efficiency values				
Vessel ID	**Vessel**	25.65 keV	48.91 keV	57.19 keV	74.56 Kev	Average efficiency for vessel type
A	16 mL vial	NA	2.50E-05	2.73E-05	2.95E-05	2.71E-05
B	12 mL vial	NA	2.55E-05	2.77E-05	2.99E-05	
C	16 mL vial	NA	2.51E-05	2.73E-05	2.97E-05	
D	23 mL vial	NA	2.39E-05	2.62E-05	2.86E-05	
E	5 mL syringe	NA	3.17E-05	3.30E-05	3.43E-05	3.34E-05
F	1 mL syringe	NA	3.25E-05	3.38E-05	3.50E-05	
Average of vial and syringe type efficiencies						3.02E-05
Absolute difference between average efficiency of vial (A to D) and syringe (E to F) vessel types						6.27E-06
% difference between average efficiency of vial (A to D) and syringe (E to F) vessel types						20.73%

Appendix 1: ^{161}Tb Sample vessel measurements and information

Table 6: Approximate measured or estimated values (mm) for vials used in revised ISOCS geometry model for Falcon 5000 measurements.

<table>
<tr><th>Geometry</th><th>Wall thickness (mm)</th><th>Bottom vial thickness (mm)</th><th>Inside diameter (mm)</th><th>Fill height 0.5 g** solution ^{161}Tb (mm)</th><th>Fill height 6 mL solution ^{161}Tb (mm)</th><th>Material density chemical composition (Jiangsu Huayi Technology Co.,Ltd 2022)</th></tr>
<tr><td>23 mL vial</td><td>1.28</td><td>1.84</td><td>27.51</td><td>1.65</td><td>NA</td><td rowspan="3">Material:
Borosilicate glass
Chemical composition:
72.85% SiO_2 ***
10.2% B_2O_3
5.8% Al_2O_3
1.2% CaO
1.5% BaO
7.3% Na_2O
1.1% K_2O
0.05% Fe_2O_3
Density: 2.36 g/cm^3</td></tr>
<tr><td>16 mL vial*</td><td>1.16</td><td>1.55</td><td>23.18</td><td>1.44</td><td>15.5</td></tr>
<tr><td>12 mL vial</td><td>1.04</td><td>1.26</td><td>23.33</td><td>1.74</td><td>NA</td></tr>
</table>

* 16 mL vial measurements based on average of 23 and 12 mL vial measurements

** Assumes density of 1.0 for ^{161}Tb solutions

***Extra 0.15% SiO_2 added to chemical composition so chemical composition adds up to 100%

Table 7: Approximate measured or estimated values (mm) for syringes used in revised ISOCS geometry model for Falcon 5000 measurements.

Geometry	Wall thickness (mm)	Inside diameter (mm)	Fill height 0.5 g solution ^{161}Tb (mm)	Material density chemical composition (Rogers, 2015)
1 mL syringe	2.35	4.86	29	**(BD, Rogers 2015)** **Material:** Polycarbonate **Chemical composition:** 100% C15H16O2 **Density:** 1.19 g/cm^3
5 mL syringe	0.6	12.87	4	**(Terumo 2022, Byju's 2022)** **Material:** Polypropylene **Chemical formula:** 100% C3H6 **Density:** 0.891 g/cm^3

Appendix 2: Screen shots of ^{161}Tb sample spectrums

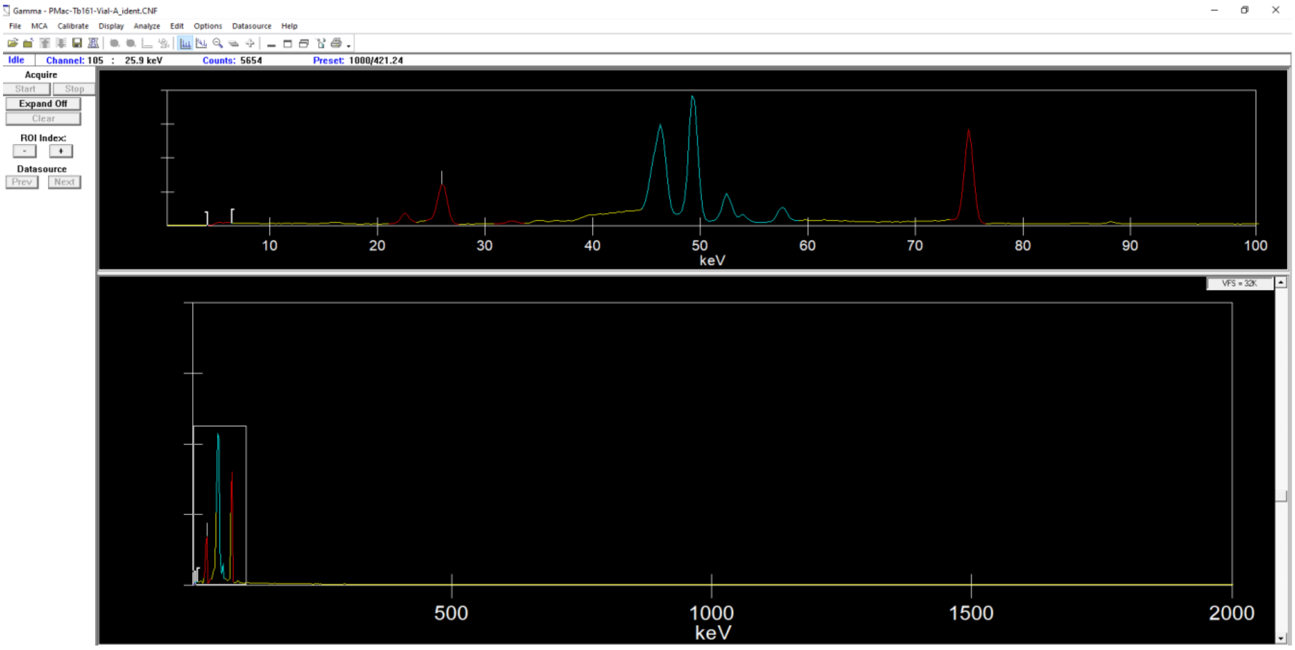

Figure 4: Screenshot of Vessel ID A spectrum, 16 mL vial with approximately 6 mL ^{161}Tb solution.

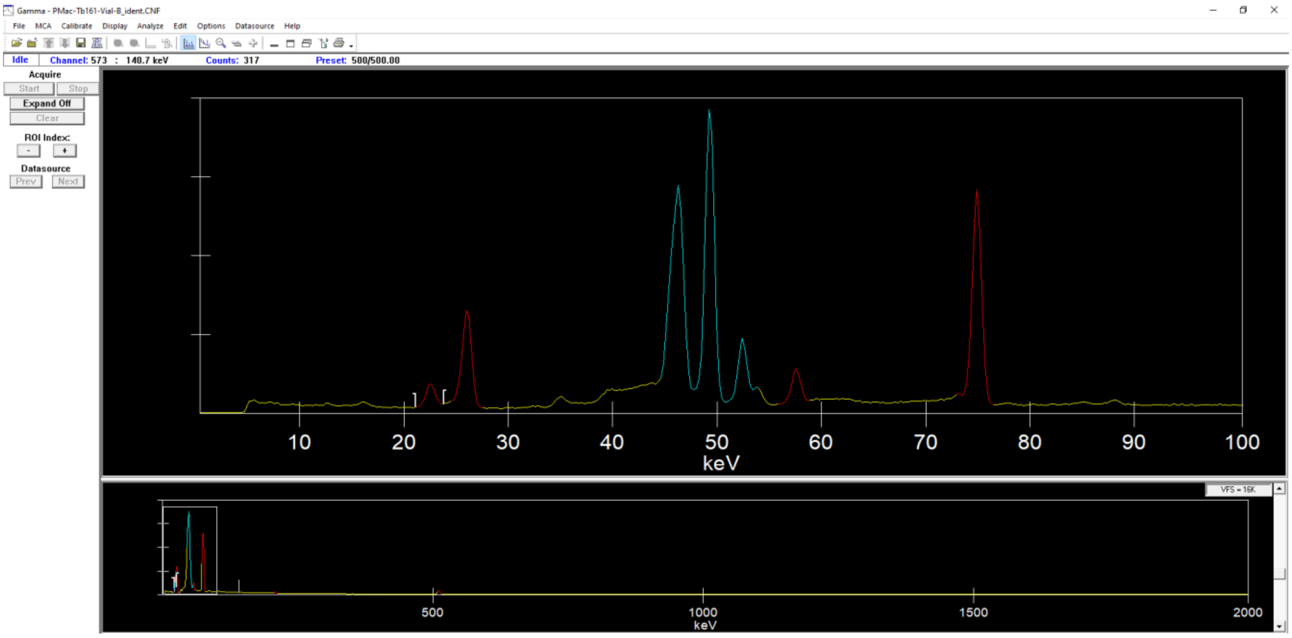

Figure 5: Screenshot of Vessel ID B spectrum, 12 mL vial with approximately 0.5 mL ^{161}Tb solution.

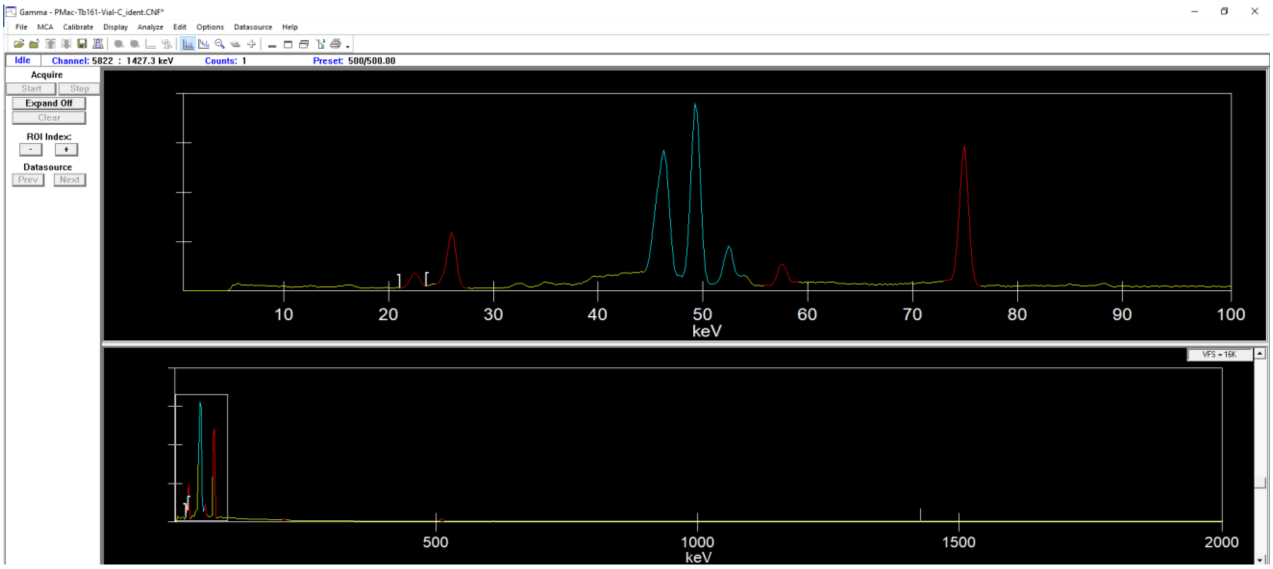

Figure 6: Screenshot of Vessel ID C spectrum, 16 mL vial with approximately 0.5 mL ^{161}Tb solution.

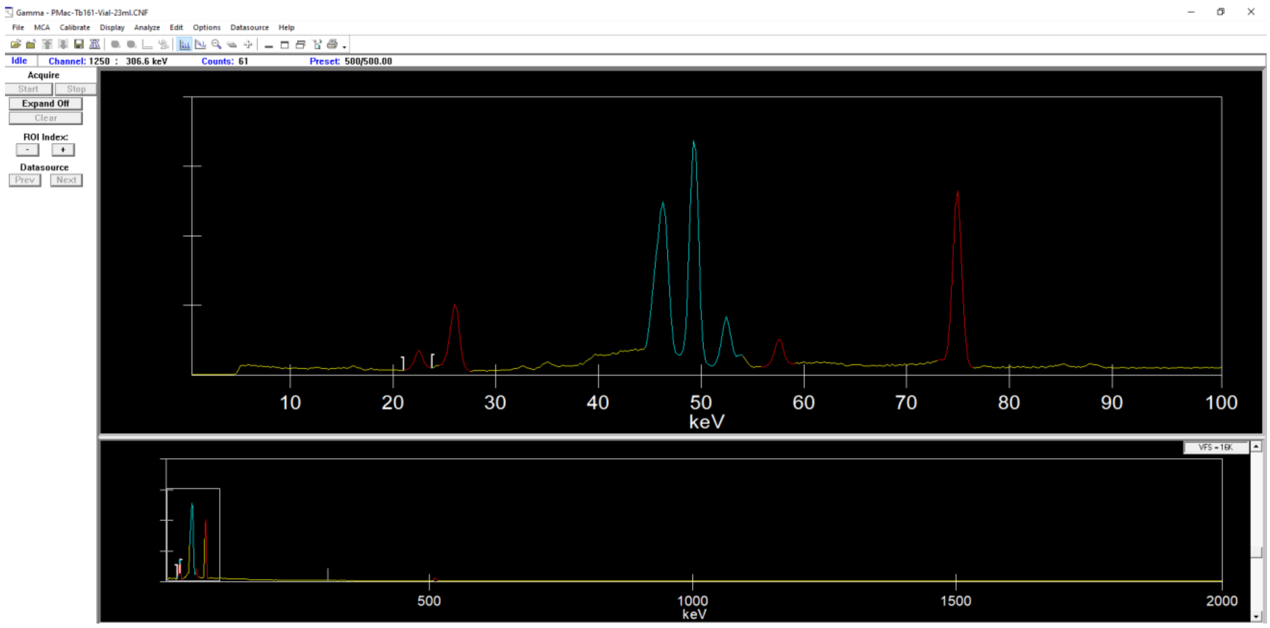

Figure 7: Screenshot of Vessel ID D spectrum, 23 mL vial with approximately 0.5 mL ^{161}Tb solution.

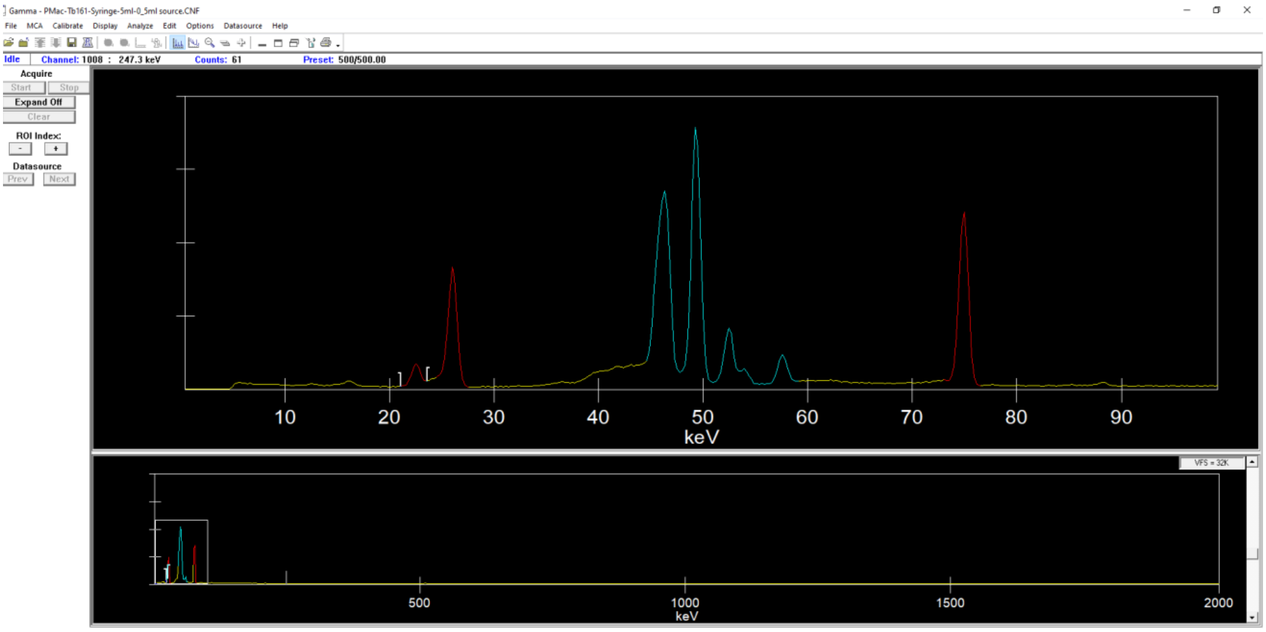

Figure 8: Screenshot of Vessel ID E spectrum, 5 mL syringe with approximately 0.5 mL ^{161}Tb solution.

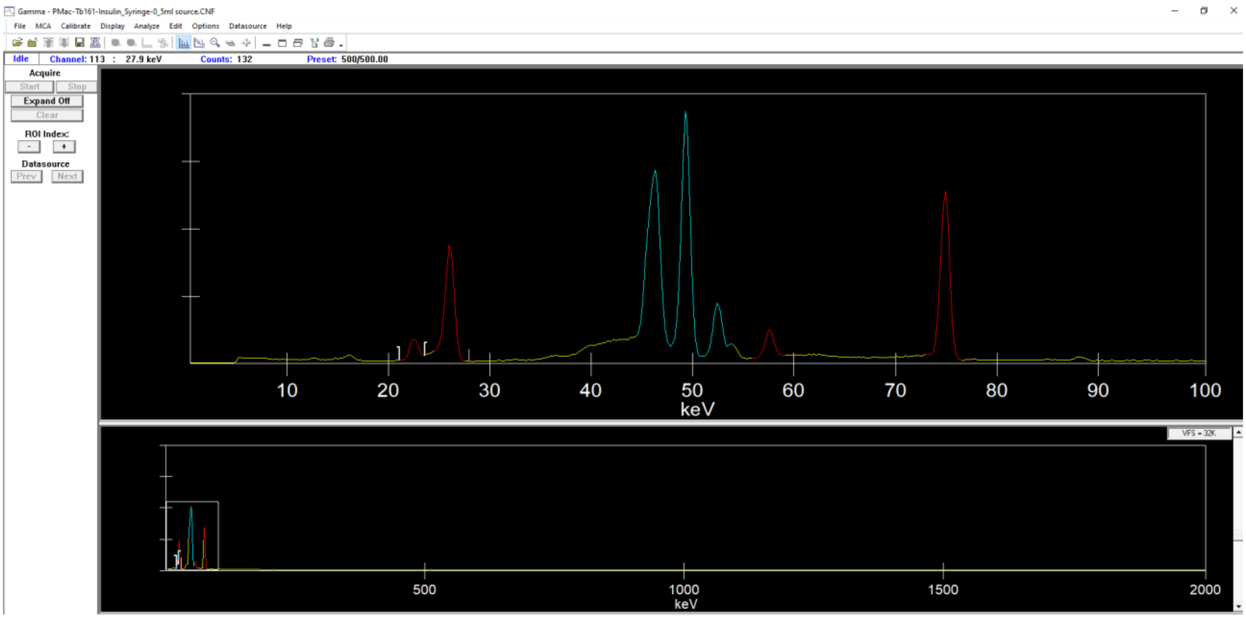

Figure 9: Screenshot of Vessel ID F spectrum, 1 mL syringe with approximately 0.5 mL ^{161}Tb solution.

Appendix 3: Glossary

Activity	The rate at which spontaneous transformation occurs in a given amount of radioactive material
ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
BD	Stands for Becton Dickinson, which is a brand of syringes
Genie 2000	A gamma spectrometry software package used for spectrum acquisition and analysis
HPGe	High purity germanium detector
In situ gamma spectrometry	Gamma ray measurements taken close to the source. Direct measurements of ground contamination in the field
In-growth	Increased relative concentration as one radionuclide transforms into another
ISOCS	In situ object counting system. A source-less calibration method where the response function of the detector is combined with user defined geometry measurements to create an efficiency calibration curve
Isotopes	Forms of the same element having identical chemical properties but different atomic masses and nuclear properties
PMCC	Peter MacCallum Cancer Centre, Melbourne Victoria
Radionuclide	A radioactive nuclide

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