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Conditioning residual radioactive Eu impurities from vials of ^{153}Sm radiopharmaceutical

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Introduction

Quadramet is a therapeutic radiopharmaceutical containing ^{153}Sm (samarium-153, $t_{1/2}$ = 1.93 days) used to attenuate the pain in palliative care of bone cancer patients. ^{153}Sm is a beta-emitting radionuclide produced by neutron activation in a reactor, accompanied by co-production of γ-emitting radioactive isotopes of Eu (europium). Despite chemical separation, trace amounts of ^{152}Eu ($t_{1/2}$ = 13.6 years), ^{154}Eu ($t_{1/2}$ = 8.6 years), ^{155}Eu ($t_{1/2}$ = 4.7 years) isotopes are present in the radiopharmaceutical. These long-lived impurities pose a challenge for elimination of spent Quandramet vials, as well as of unused radiopharmaceutical. The Radioanalytical Chemistry Group (GCR) of the Institute of Radiation Physics (IRA) examined the feasibility of concentrating these residual Eu impurities on a single ion-exchange column with a prospect to discharge empty vials with non-radioactive waste.

Radiopharmaceutical vials

GCR received 50 vials of expired Quadramet with radioactivity of ^{153}Sm largely decayed. Some vials seem unused and are filled with approx. 2-3 mL of yellow liquid. Some vials were likely used only partly, containing residual yellow liquid in volume inferior to the volume indicated on the label. Some vials are empty. In some vials, the product solidified into a yellow resinous substance, distributed unevenly within the vial (*e.g.* stuck near the rubber cap).

Experimental Setup

Chemicals and equipment

- DGA-Normal resin 2 mL cartridge (Triskem, ref. DN-R10-S, lot FDNS201005, 50-100 µm particles, produced 05.10.2020)
- Mini-Spike® Chemo vented with filter (B. Braun, ref. 4550340, lot 21C04A8131, exp. 01.03.2026)
- Peristaltic pump Ismatec® IPC 12
- Nitric acid 4 M HNO_3
- Osprey NaI scintillation radioactivity detector
- Disposable syringe 5 mL

Procedure

A single DGA cartridge was conditioned by passing 10 mL of 4 M HNO_3 at 1 mL min^{-1} flow rate using a peristaltic pump. This cartridge was used to successively load the contents of Quadramet vials used in this experiment.

1. 5 mL of 4 M HNO_3 were injected in a Quadramet vial using a vented Mini-Spike® (Figure 1).
2. This was followed by solubilising the contents by thoroughly shaking the vial.
3. Then, the solubilised residue was removed through a vented Mini-Spike® using a 5-mL syringe.

4. The solubilised residue was loaded on DGA column using a peristaltic pump at 1 mL min^{-1} flow rate, collected flow-through.
5. The radioactivity of the empty vial was then measured using NaI Osprey detector.
6. Repeated washing step were carried out using 5 mL 4 M HNO_3.
7. The radioactivity of the empty vial, of the DGA column, and of the collected flow-through from each individual vial was measured.
8. The radioactivity of the empty vials was additionally measured using a HPGe detector.

Figure 1. A vented Mini-Spike® Chemo with filter enabled safe injection of 4 M HNO_3 in a spent Quadramet vial without loss of radioactivity to the environment. Withdrawal of solubilised Eu from the vial was carried out using the same Mini-Spike®, minimising contamination risk through reduced amount of material.

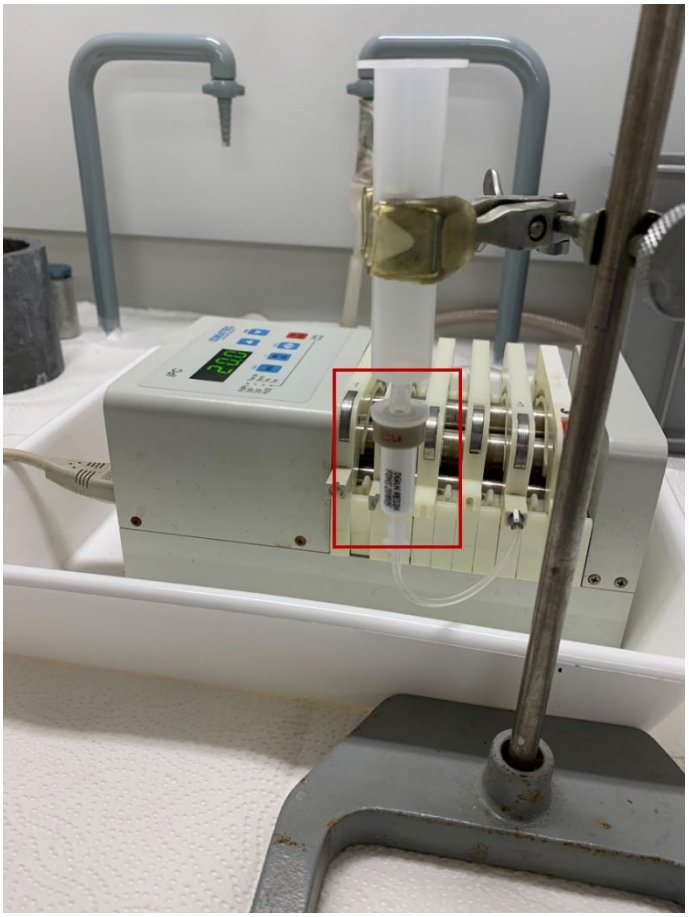

Figure 2. A DGA column containing approx. 4 KBq of ^{152,154,155}Eu extracted from five Quadramet vials. Solubilised residue was transferred from vials using a peristaltic pump at 1 mL min^{-1} flow rate.

Results and discussion

Five vials were selected randomly to test the extraction and conditioning of residual radioactivity (Table 1). Initial examination of the labels provided expiration dates of the radiopharmaceutical (years 2000-2005), enabling to exclude radioactivity of ^{153}Sm that had largely decayed since. Gamma spectrometry done on one of the vials, using an HPGe detector, identified three isotopes of europium – ^{152}Eu, ^{154}Eu and ^{155}Eu – as residual radioactive impurities (Table 2). Visual examination of the vials revealed the presence of traces of yellow resinous residue, or yellow liquid in some vials.

Table 1. Quadramet vials selected for conditioning residual radioactivity. Initial radiopharmaceutical concentration of ^{153}Sm stated on the label was 1.3 GBq mL^{-1}.

	Lot nr.	Original V, mL	Exp. date	Volume in vial as received for measurement
Vial 7	5060-55	2.16	11.08.2005	Empty
Vial 8	4032-49	2.31	29.04.2004	Approx. 2 mL yellow liquid
Vial 9	T008-10	2.16	31.01.2000	Approx. 0.5 mL of solidified resinous yellow substance near the cap
Vial 13	4070-58	3.08	30.09.2004	Empty
Vial 15	4064-52	3.08	09.09.2004	Empty

Table 2. Residual radioactivity determined in one representative vial. Vial 7 was measured using an HPGe detector prior to conditioning, and after removal of residual radioactivity.

	^{152}Eu, Bq	^{154}Eu, Bq	^{155}Eu, Bq	Total, Bq
Vial prior to wash	723±15	1164±18	89±7	1976±25
Vial washed	4±1	7±1	*below det. limit*	11±2

Chemical composition of the residue present in the vials is essential for quantitative removal of Eu, as well as for efficient extraction of Eu on DGA resin. According to the SPC, Quadramet contains a complex of ^{153}Sm with ethylene diamine tetramethylene phosphonate (EDTMP) at pH 7-8.5 in the presence of calcium and sodium. EDTMP is a strong chelating agent. Therefore, to break down the complexes of residual Eu with EDTMP, a strong acidic solution is necessary in order to quantitatively transfer Eu on DGA resin. In addition, extraction of Eu on DGA resin is most efficient from 3 M – 4 M HNO_3, with resin capacity factor (k') in the range of 10^3-10^4.[1] These conditions showed favourable outcome and nearly quantitative removal of Eu isotopes from vials tested in this experiment (Table 3).

Table 3. Residual radioactivity of conditioned Quadramet vials. Determined with a NaI scintillation detector (counts) as a guidance only because of different geometries. Final quantitative measurement (Bq) were carried out using an HPGe detector.

	background, counts	vial, counts	wash 1, counts	wash 2, counts	wash 3, counts	HPGe, Bq ^{152}Eu+^{154}Eu
Vial 7	2075	n/a	2'325	n/a	n/a	10.57
Vial 8	2425	1'9675'42	7'062	6'038	n/a	119.4
Vial 9	2612	113'008	10'480	2'612	n/a	13.5
Vial 13	2371	1'243'483	28'478	3'820	3'070	11.8
Vial 15	2295	117'999	4'703	2'746	n/a	6.7

Table 3 shows that 2 x 5 mL wash with 4 M HNO_3 was sufficient to solubilise and remove most of Eu radioisotopes, reducing radioactivity of the vial to nearly background. A third washing step tested with one vial (table 3, vial 13) resulted only in a small reduction of radioactivity, from 3820 to 3070 counts, and can be omitted as its benefit is insignificant. Gamma spectrometry of vial 7 (table 2) showed that solubilisation and extraction with 4 M HNO_3 enabled reduction of residual radioactivity by a factor of at least 10^3, from 1976±25 Bq to 11±2 Bq. Noteworthy, ^{155}Eu present in all vials prior to conditioning was below the detection limit after vials were washed.

According to Radiological Protection Ordinance (ORaP), clearance limit (LL) for both ^{152}Eu and ^{154}Eu is 0.1 Bq g^{-1} (ORaP, annex 3). Articles 106 and 111 of ORaP allow discharge to the environment of <10 kg*LL (Bq $week^{-1}$) without the approval of the licensing authority. For ^{152}Eu and ^{154}Eu this equals to <1000 Bq $week^{-1}$. Total radioactivity of residual ^{152}Eu and ^{154}Eu determined with HPGe (table 3) in each vial is below 20 Bq, with exception of vial 8 containing 119.4 Bq. Nevertheless, these vials can be cleared for discharge to the environment, taking into account the total inventory of other radioactive waste produced by the license holder.

Loading radioactive Eu on DGA resin enables to concentrate radioactive waste from a large number of vials on a single column. However, it is essential to ensure that successive loading of multiple samples does not result in a breakthrough of Eu radioactivity at some point of saturation. The capacity of DGA resin for Eu (III) is 0.077 mmol mL^{-1}, meaning that a 2-mL DGA column can extract up to 1.5×10^{11} Bq of ^{152}Eu or 2.4×10^{11} Bq of ^{154}Eu. This capacity is largely sufficient to condition residual Eu from Quadramet vials. Large volume of 4 M nitric acid pumped through the column may also result in a breakthrough of Eu. In this experiment, approx. 150 mL of 4 M HNO_3 passed through a single DGA column during various optimisation steps without loss of radioactivity from the column. An optimised protocol would require approx. 10-15 mL of 4 M HNO_3 to condition each vial, thus minimising the risk of Eu breakthrough due to large acid volume.

The total radioactivity of the DGA column following the transfer of residual Eu from five Quadramet vials in this experiment was estimated at approx. 4 kBq, requiring a specific authorised disposal.

Conclusion

Commercially available DGA cartridge enabled to concentrate residual radioactive Eu impurities from spent Quadramet vials. Conditioning the vials with 4 M HNO_3 reduced residual radioactivity

below the LL allowing the discharge to the environment. Based on the protocol tested in this study, GCR can propose two options for conditioning radioactive waste from spent Quadramet vials.

1. A centralised collection of all spent vials and conditioning in a licensed laboratory, *e.g.* GCR-IRA, followed by disposal of concentrated radioactive Eu waste. This solution would involve the transport of radioactive materials to and from IRA, and a workforce for processing the vials and eventually a disposal of the radioactive waste at PSI.

2. Individual conditioning of spent vials on site by medical centres using a detailed protocol and a kit provided by GCR. Such protocol would require manual handling of each spent vial and loading samples on the DGA cartridge using a syringe. There is a possibility to replace syringes with evacuated vials, which can aspirate the sample through the DGA column. However, this option requires additional testing because the flow rate provided by an evacuated vial may not be suitable for quantitative extraction of Eu on DGA resin. In addition, this option may be integrated into the routine radioactive waste management at medical centres using ^{153}Sm enabling immediate discharge of spent Quadramet vials. Activity determination of spent and washed vials is still necessary prior to discharge.

References

1. E. P. Horwitz, D. R. McAlister, A. H. Bond & R. E. Barrans Jr (2005) Novel Extraction of Chromatographic Resins Based on Tetraalkyldiglycolamides: Characterization and Potential Applications, Solvent Extraction and Ion Exchange, 23:3, 319-344, DOI: 10.1081/SEI-200049898