

SECURE

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“Target requirements (quantities and quality) and sourcing for existing and foreseen irradiation infrastructure for production of alpha-emitting radionuclides”

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EXECUTIVE SUMMARY

This deliverable considers different target requirements for the various routes towards ^{225}Ac production. ^{223}Ra and ^{212}Pb production is covered in the regard where there is overlap, especially with regards to similarities in requirements for ^{226}Ra target manufacture.

The initial part of this deliverable considers what has been published in the literature, what an expected quantity of material is, or could be, and how this is formed into a target for irradiation.

The type of target required is dictated by the facilities available including the irradiation device, and considerations around size, shape, backing material and chemical form are evaluated. This deliverable contributes to the wider aim of interchangeable targets across multiple irradiation devices within the consortium.

A theoretical nuclear physics evaluation of the potential routes to ^{225}Ac via the various accelerator and reactor routes will be captured elsewhere, and should be referred to in order to complement this deliverable.

The target requirements that have been considered for routes to ^{225}Ac production are: legacy material via decay, proton irradiation, deuteron irradiation, gamma irradiation and by neutron irradiation (thermal and fast). Targets for ^{223}Ra production consider routes from legacy material via decay and potentially by utilising by-products of other irradiations. Targets for routes for ^{212}Pb production considers legacy material via decay and by neutron irradiation of ^{226}Ra .

The predominant irradiation target for these materials is ^{226}Ra regardless of irradiation type, either through single or multiple events, transmuting to ^{225}Ac directly or creating isotopes higher up in the decay chain and time given to decay. Potential legacy sources of ^{226}Ra , and their expected impurities, have been presented, but will be more fully extrapolated in other tasks.

The pre-processing of target material and the post-processing of irradiated targets is not covered in this deliverable but is anticipated to be covered elsewhere within the overall programme of work.

Quantities, where given, are presented of ^{226}Ra sources, and different potential chemical forms of radium are discussed, with their challenges and benefits. A brief introduction to some of the challenges of working with ^{226}Ra have been explored, but this is closely tied into infrastructural requirements which will be more fully covered in D1.2.

Information has been captured around the irradiation facilities available at NRG and at ILL, and some of the physical and logistical considerations described should a target be envisaged to be prepared and/or irradiated at those facilities.

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1 INTRODUCTION

This deliverable 1.1 sets out to describe “*Target requirements (quantities and quality) and sourcing for existing and foreseen irradiation infrastructure for production of alpha-emitting radionuclides*”. This work is undertaken and captured in work package 1, task 1.2.

To enable a realisation of SECURE’s aims to ‘make a major contribution to the sustainability of medical isotope production and its safe application in Europe’ key alpha emitters have been selected to evaluate the challenges of sourcing, production and use. This is a multifaceted challenge, as alpha-emitting materials predominantly need specialist infrastructure and handling.

Through this task, key alpha-emitters have been selected, their production routes evaluated, and the target requirements for each type described. Where experimental results, including quantity of target material and yields have already been reported, these have been captured. Data has been obtained from both literature and partners’ experience in this area.

Sourcing of target materials, where not by standard commercial procurement, such as in the case of proposed target material ^{226}Ra , will be more comprehensively discussed in task 1.3 (D1.3) and task 1.9 (D1.9). Infrastructural considerations relating to handling of the target material (especially with regard to the alpha-emitting ^{226}Ra target material) will be covered more extensively in task 1.1 (D1.2). Some of the discussions and outcomes of this (D1.1) report are likely to be of use in covering a part of task 1.4 (D1.4) for consideration of the target requirements for ^{226}Ra use in non-reactor irradiation devices.

Set out in this deliverable are potential and demonstrated routes to production of identified key alpha-emitting radioisotopes for medical use. WP2 (task 2.1) sets out an ambition to identify the ‘availability / capacity of current methods for α -emitters production by thermal neutron spectrum reactors.’ Within the SECURE proposal, ^{225}Ac is named as the main radionuclide of interest, therefore identification of production routes to ^{225}Ac using thermal neutron spectrum reactors will be the main focus of this task. Within WP2 and the introduction, ^{212}Pb is mentioned as a radioisotope of interest, alongside ^{223}Ra mentioned as “the first alpha emitter which has been granted marketing authorization”. Therefore, this task will focus on target requirements and preparation of ^{225}Ac , with some considerations towards production of ^{212}Pb and ^{223}Ra where there is applicable learning, for example using ^{226}Ra as a starting material, or using by-products of the ^{225}Ac -producing irradiation route.

Actinium-225 (^{225}Ac), radium-223 (^{223}Ra) and bismuth-212 (^{212}Bi) are all of interest as α -particle emitting isotopes for medical therapeutic systems such as targeted alpha therapy (TAT). As ^{212}Bi has a half-life of 60.55 minutes [1], to enable sufficient time to undertake radiopharmaceutical production, a more common delivery system is often proposed *via* a lead-212 (^{212}Pb)-loaded radiopharmaceutical, which decays via β -decay with a half-life of 10.62 hours, creating an *in-vivo* generator of ^{212}Bi . The longer half-life ^{225}Ac ($T_{1/2} = 9.92$ d) and ^{223}Ra ($T_{1/2} = 11.4$ d) means that a progenitor *in-vivo* nuclide is not envisaged. Therefore, most production routes will envisage the potential and demonstrated routes to ^{225}Ac with consideration also of routes ^{223}Ra , ^{212}Pb (and not ^{212}Bi).

Set out in this report are the target requirements, where reported in the literature, or fed back from partners, for generation of these radionuclides through existing or foreseen irradiation infrastructure.

2 TABLES OF ROUTES TO ACTINIUM-225, RADIUM-223 AND LEAD-212

Table 1. Table of potential routes to ²²⁵Ac

#	Source	Target	Annual Capacity	225Ac production	Challenges	Advantages	Irradiator device /within SECURE
1	Legacy material via decay	229Th decay	720 mCi/year (ORNL); ~720 mCi/year (Russia); 350 mCi/year (ITU)	229Th → 225Ra (T _{1/2} = 14.9 d) → 225Ac (T _{1/2} = 9.92 d)	Limitation of 229Th availability	Well-established process and clinical pedigree; Highly pure product	n/a
2a	Proton Irradiation	226Ra	13 mCi of 225Ac after irradiation of 30.1 mg 226Ra with ~16 MeV protons for 45.3 h	226Ra(p,2n)225Ac	226Ra handling; 226Ra availability	Maximum cross section of 710 mb at 16.8 MeV; Similar purity of end product as 229Th source. Proton energies below 20 MeV needed	
b	Proton Irradiation	232Th	~2 Ci (LAN/BNL) over 10 days of target irradiation	232Th(p,4n)229Pa; 229Pa (T _{1/2} = 1.54 d) → 229Th decays as #1 to 225Ac	227Ac contamination at "0.1%-0.2% activity" [2]; Elaborate chemical separation from many isotopic byproducts. 20-200 MeV proton energy (DOE tri-lab: 100-1400 MeV with beam currents up to 250 uA) 227Ac (T _{1/2} =21.8 years) levels of 0.1%-0.2% activity (EOB)	End product pure enough for TAT research application	DOEs tri-lab and TRIUMF also in Troitsk
c	Proton Irradiation	230Th		230Th(p,2n)229Pa; 229Pa (T _{1/2} = 1.54 d) → 229Th decays as #1 to 225Ac			
3	Deuteron Irradiation	226Ra		226Ra(d,3n)225Ac	Theoretically modelled. 18.5 MeV energy required		
4a	Gamma Irradiation	226Ra	11 μCi or 225Ra/h/20mCi of 226Ra	226Ra(γ,n)225Ra; 225Ra (T _{1/2} = 14.9 d) → 225Ac	Production method requires R&D; 226Ra availability and handling. Threshold is at 6.4 MeV (Argonne), max cross section at 532 mb at energy 13.75 MeV.	Potential for high yields and high product purity	LINAC proposed LEAF at Argonne
b	Gamma Irradiation	230Th		230Th(γ,n)229Th	Theoretically proposed. Th isotopes can pose separation challenges.		
5a	Neutron: Thermal (E < 1eV)	226Ra (or 228Ra)	Strongly dependent on availability of 226Ra	226Ra(n,y)227Ra; 227Ra (T _{1/2} = 42.2 m) → 227Ac; 227Ac(n,y)228Ac; 228Ac (T _{1/2} = 6.15 h) → 228Th; 228Th(n,y)229Th; decays as #1 to 225Ac	Three neutron capture process, plus time needed to decay. ~0.025 eV electron flux needed. Limitations include unfavourable neutron cross sections for some intermediates. Co-production of significant quantities of 228Th		
5bi	Neutron: Fast (E > 10keV)	226Ra (or 228Ra)	Strongly dependent on availability of 226Ra	226Ra(n,2n)225Ra, then 225Ra (T _{1/2} = 14.9 d) → 225Ac	Significant amount of 226Ra needed, 228Th produced. Yield potentially limited by neutron capture of 225Ra. Estimated neutron energies ~12MeV, although limited underpinning data	Significant production capacity for 225Ac	
bii	Neutron: Fast	230Th		230Th(n,2n)229Th	Theoretically proposed. Threshold value of 6.4 MeV		

Table references:

Table adapted from Birnbaum *et al.* Actinides in Medicine. Encyclopedia of Inorganic and Bioinorganic Chemistry [2].

Other additions:

Mirzadeh/Battelle LLC Production of thorium-229 using helium nuclei Patent number US7852975B2 [3]

Papers: Perron *et al.* [4], Hogle *et al.* [5], Boll *et al.* [6]; Kuznetsov *et al.* [7], Iwahashi *et al.* [8]

Table 2. Table of potential routes to ²¹²Pb

#	Source	Target	Annual Capacity	²¹² Pb production	Challenges	Advantages	Irradiator device /within SECURE
8	Legacy material via decay	²³² U, ²²⁸ Th or ²³² Th decay	Capacity limited by historic source material	<p>²³²Th (1.4×10^{10} y) → ²²⁸Ra ($T_{1/2} = 5.75$ y) → ²²⁸Ac ($T_{1/2} = 6.15$ h) → ²²⁸Th</p> <p>²³²U ($T_{1/2} = 68.9$ y) → ²²⁸Th</p> <p>²²⁸Th ($T_{1/2} = 1.91$ y) → ²²⁴Ra ($T_{1/2} = 3.63$ d) → ²²⁰Rn ($T_{1/2} = 55.6$ s) → ²¹⁶Po ($T_{1/2} = 0.145$ s) → ²¹²Pb ($T_{1/2} = 10.64$ h)</p>	Limitation of ²³² U or ²³² Th availability. Ability to handle of large amounts of uranium or thorium needed.	No irradiation required. Complex multi-step purification needed of raw material	n/a
9	Neutron Irradiation	²²⁶ Ra	Strongly dependent on availability of ²²⁶ Ra and the chemical form in which the radium is irradiated.	<p>²²⁶Ra(n,y)²²⁷Ac; ²²⁷Ac(n,y)²²⁸Th; ²²⁸Th → ²¹²Pb as per #8</p>	²²⁶ Ra handling, ²²⁶ Ra availability		

Table references:

ANL report [9], IAEA TechDoc-1630 [10], Kirby *et al.* [11]

Table 3. Table of potential routes to ²²³Ra

#	Source	Target	Annual Capacity	223 Production	Challenges	Advantages	Irradiator device /within SECURE
10a	Legacy material via decay	²³¹ Pa source	Capacity limited by historic source material, and rate of grow-in of decay chain	²³¹ Pa (T _{1/2} = 3.28 × 10 ⁴ y); → ²²⁷ Ac	Material handling challenges. Access to material is limited and costly. Long half-life of the parent.	Does not require irradiation	
10b		Historic ²²⁷ Ac-Be neutron sources	Capacity limited by historic source material, and rate of grow-in of decay chain	²²⁷ Ac (T _{1/2} = 21.7 y); → ²²⁷ Th (T _{1/2} = 1.9 y); → ²²³ Ra	Limited availability of historic ²²⁷ Ac-Be neutron sources. Material handling challenges. Access to material is limited and costly. Long half-life of the parent.	Does not require irradiation	
11a	Irradiation	²²⁶ Ra	Dependant on availability of ²²⁶ Ra and yields of ^{Ac227} formed	²²⁷ Ac is a by-product of ²²⁶ Ra(p,2n), ²²⁶ Ra(d,3n) ²²⁶ Ra(γ,n) and ²²⁶ Ra(n,2n) routes ²²⁷ Ac (T _{1/2} = 21.7 y); → ²²⁷ Th (T _{1/2} = 1.9 y); → ²²³ Ra	Radiochemical separation of ²²³ Ra from ²²⁷ Ac and ²²⁷ Th.	²²⁷ Ac can either be the main product or a by-product from ²²⁸ Th or ²²⁵ Ac production. Claimed 'high purity'.	
11b	Proton Irradiation	²³² Th	Dependant on availability of ²²⁶ Ra, ²²⁵ Ac production, and yields of ²²⁷ Ac by-products formed	²²⁷ Ac (T _{1/2} = 21.7 y); → ²²⁷ Th (T _{1/2} = 1.9 y); → ²²³ Ra	Via ²²⁷ Ac by-products produced by irradiation.	By-product of ²²⁵ Ac production.	

Table references

Soderquist *et al.* [12], Abou *et al.* [13],

Larsen/Bayer AG Preparation and Use of Radium-223 to Target Calcified Tissues for Pain Palliation, Bone Cancer Therapy, and Bone Surface Conditioning Patent number US6635234B1 [14]

3 TARGET REQUIREMENTS FOR PRODUCTION ROUTES

This section will detail the target requirements for materials used within the production routes listed in Table 1, Table 2 and Table 3.

3.1 Method 1 – Legacy Material

No targets required for irradiation, however one established method of production of ^{225}Ac from legacy material is through separation from ^{229}Th , a long lived ($T_{1/2} = 7340 \text{ y}$) radionuclide within the fissile ^{233}U decay chain.

Methods for the separation and purification of extracted ^{225}Ac are well reported, with the extraction of ^{229}Th from ^{223}U stock material being achieved through anion exchange (Dowex 1x8, 100-200 mesh) of the material in 8M HNO_3 to remove ^{233}U , ^{225}Ra and ^{225}Ac , with ^{229}Th being eluted in 0.1M HNO_3 [15]. The ^{229}Th source can then be held in solution and cycled through an anion exchange column (Dowex 1x8, 100-200 mesh) for removal of ^{225}Ac and ^{225}Ra daughters. The eluate is passed through a prefilter column to remove organic contaminants and placed through a second anion exchange column to remove small amounts of Th contaminants. Separation and purification of ^{225}Ra and ^{225}Ac can be achieved through extraction chromatography columns (UTEVA and RE-resin) [15].

This production method is limited by the availability of source material, the largest stocks were typically generated through neutron irradiation of ^{232}Th for weapons programmes in the 1960's and 1970's. It is estimated that existing sources of ^{229}Th worldwide, are capable of supplying around 69 GBq ^{225}Ac per annum for pre-clinical and clinical use [16].

3.2 Accelerator Targets Summary

Targets are designed to accommodate the material being irradiated. In contrast to target material for neutron irradiation in a nuclear reactor, which are sealed in quartz ampules, accelerator's (cyclotron's) target material is directly exposed to the irradiating particles under vacuum. Due to this fact, preparation is more challenging.

Target system production capacity is a function of the incident beam current and energy. The charged particles hitting the target lose energy rapidly producing waste heat, which need to be removed from the system to sustain its operation. The power in watts is equal to the energy deposited (MeV) multiplied by the beam current (in μA). For example, a thick target which degrades a proton beam 15 MeV at 100 μA , absorbs 1,500 W in a few square centimetres [17]. Therefore, in order to prevent target overheating and possible destruction, a major concern in target design is the generation and dissipation of heat during irradiation. Efficient cooling not only ensures that the target material will remain in the target but also allow the target to be irradiated at higher beam currents, which in turn allows production of more radioisotopes in a given time.

In addition, target material itself must be able to withstand the heat deposited during the irradiation. Targets are therefore expected to have good thermal conductivity and high melting points. Target thickness must correspond to the energy range favouring the reaction of interest and reducing the production of contaminants. Moreover, the higher the purity of the target material the lower the risk of contamination with charged particle-activated impurities. In addition, higher specific activities are obtained using enriched target materials. Therefore, enriched materials are preferred over natural ones.

The chemical form of the target material in addition to being durable and resistant to a high current beam, are expected to allow a feasible post-irradiation processing and high efficiency material recovery after the irradiation, when isotopically enriched target material was used.

3.3 Method 2 – Proton Irradiation (p,2n), (p,pn)

3.3.1 Method 2a: $^{226}\text{Ra}(p,2n)^{225}\text{Ac}$

3.3.1.1 Starting Material, Quantities and Chemical form

Apostolidis *et al.* [18] describe and demonstrate a route using a ‘compact medical cyclotron’ to produce ^{225}Ac via the $^{226}\text{Ra}(p,2n)^{225}\text{Ac}$ nuclear reaction. The radium for the targets used was obtained as RaCO_3 , and purified before use to remove trace ^{227}Ac . Purification methods that were used include several dissolution steps before column separation. Purity was analysed for absence of ^{227}Ac by ICP-MS. The purified radium was made up into a radium stock solution using dilute HCl.

3.3.1.2 Target Manufacture

3.3.1.2.1 Solid Targets

Apostolidis *et al.* [18] describe preparation of the small amounts of radium from a stock solution, with a solution of 10 ml of $^{226}\text{RaCl}_3$ in 0.1 M HCl prepared and used. The solution was slowly evaporated on thin silver foils and covered with a second silver foil. These silver foils were then pressed and encapsulated in silver capsules. After encapsulation, the capsules were welded to ‘gas tight’. Silver foils of different thickness were used. [18] These targets were placed in a water-cooled target holder and irradiations were performed at up to 28 MeV energy at the Karlsruhe cyclotron. [19] Cross-sections for proton energies from 9 to 25 MeV were measured by Apostolidis *et al.* [18] by chemical separation of dissolved target layers. A maximum cross-section was found to be 710 mb at a proton energy of ≈ 16.8 MeV. [19]

For targets containing larger (mg) amounts of radium, Apostolidis *et al.* [18] demonstrated a route for target production. Typically, 30 mg of radium in 0.1 HCl solution was mixed with a matrix of barium, “*due to the similar chemical properties of Ba and Ra*” [18]. The barium was typically in a ten-time excess (300 mg) of radium, in the form of a solution of BaCl_2 . The mixed solution was evaporated, and the residual solid phase was ground to powder and pressed into a pellet. The pellets were enclosed in silver capsules, and welded gas tight. Typical dimensions are quoted as “*pellet of 16 mm in diameter and 0.8–1.0 mm in height.*” [18]. A prepared target is shown in Figure 2. [19]. These thick targets were irradiated with 100 μA of protons for 1 day, with 5 GBq of ^{225}Ac produced. The maximum cross-section was found to be 10 mb at a proton energy of ≈ 16.8 MeV.

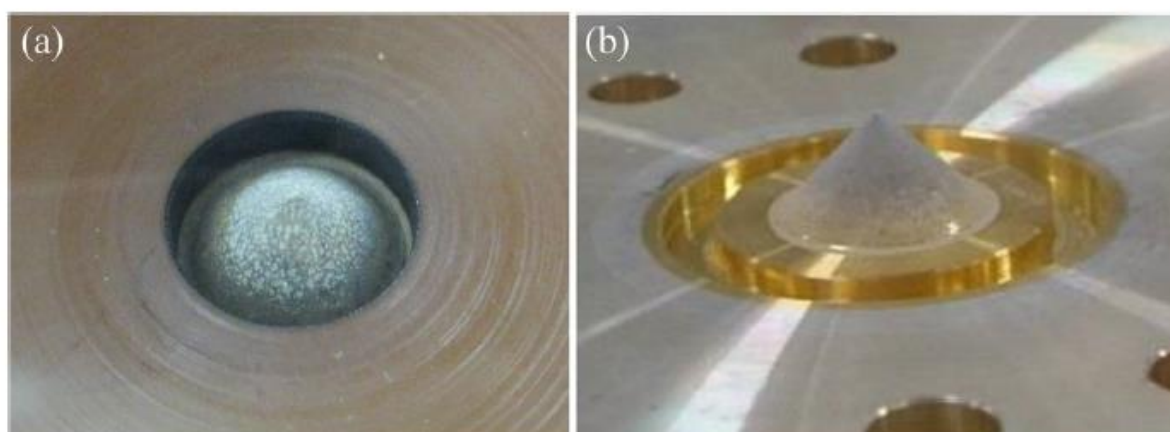


Figure 1. Deposition profile of (a) approximately 37 MBq (1 mCi) of ^{226}Ra on the target surface and (b) 5 mg of Ba. Both electrodepositions were performed under the same conditions (100 mA constant DC for 3 h) Images taken from reference [20].

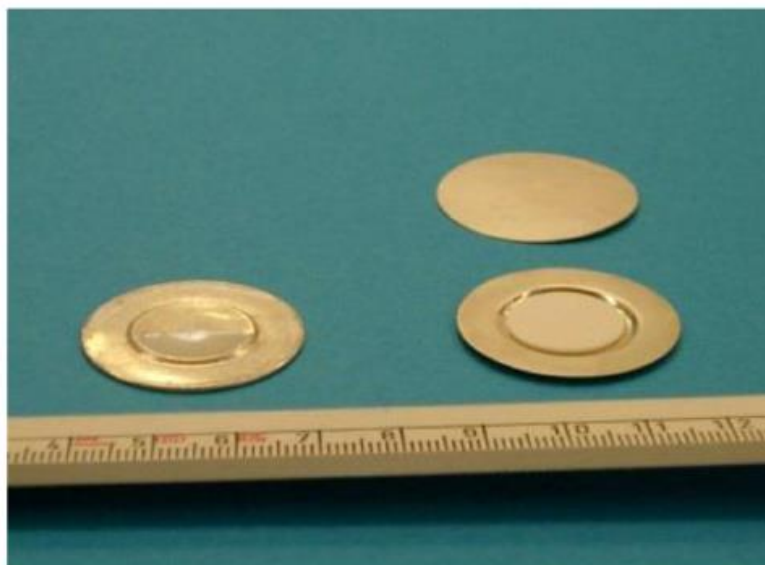


Figure 2. Photograph of a thick radium/barium chloride target prepared at JRC Karlsruhe prior to gas-tight welding. Right foreground: target disk on base of Ag enclosure; right background and left: lid and base of Ag enclosure. Image taken from reference [19].

Nagatsu et al [20] describe the radium-depositing electrolyte preparation from purified, dried ^{226}Ra , which was quantified in terms of activity. The values given for the prepared targets range from 14.8 to 38.9 MBq (400–1050 μCi).

To prepare the electrolyte, the radium was dissolved in 1 mL 0.1 M HCl and 2 mL of 0.5 M ammonium acetate. A titanium cylindrical cavity with a volume of ~ 3.5 mL was used for the electroplating reservoir and the dissolving vessel for the Ra target after activation. A platinum rod with a diameter of 3 mm was used as the anode for electroplating, and the anode was removed before the target body was sealed with a Nb foil. For chemical resistance, the conical shaped radium-depositing surface was fabricated in gold. This then underwent an electrodeposition process, rinsed, dried and resulting ^{226}Ra activity was measured.

The target apparatus (as shown in Figure 3) was sealed with a 50- μm -thick Nb foil. The yield of the process was 94-97 %. The deposited ^{226}Ra layer also contained barium, which was present as carrier from within the needles. Barium, as a comparative surrogate for radium, was also prepared from the electrodeposition method. [20] Side by side visual profiles are shown in Figure 1, which shows comparative profiles of ^{226}Ra (4a) and 5 mg Ba (4b). Quantities used were defined by activity for Ra (13.5 – 37.5 MBq ((366–1010 μCi)) and mass of Ba (5 mg).

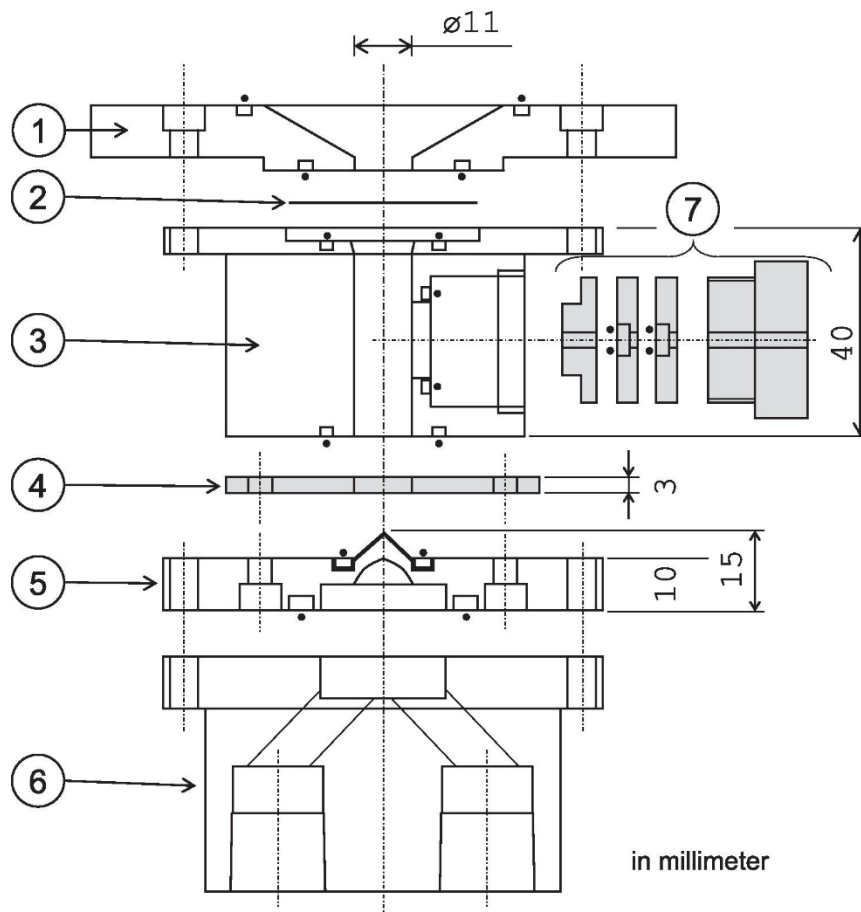


Figure 3. ^{226}Ra target box assembly. (1) beam entrance (2) $50\ \mu\text{m}$ Nb foil, (3) Ti cylindrical cavity, (4) polyimide electric insulator, (5) Silver cavity with conical shaped Ra-depositing surface, (6) not defined in paper, (7) polyimide screw with O-rings. Figure taken from reference [20]

Patent WO1999063550A1 [21] illustrates a proposed target assembly to use to irradiate ^{226}Ra in the cyclotronic production of ^{225}Ac . The chemical form of the ^{226}Ra is RaCl_2 , which was obtained from precipitation with c.HCl , or RaCO_3 . The RaCl_2 is pelletised and heated to above $150\ ^\circ\text{C}$ before irradiation in order to release crystal water. The pellets are then sealed in a capsule made of silver. Silver was chosen for its high thermal conductivity to dissipate heat generated during irradiation.

3.3.1.2.2 Liquid targets

A liquid target was proposed to produce ^{225}Ac using a ^{226}Ra chloride solution. [22] The initial investigations were undertaken using a barium surrogate, and cooled using a liquid-helium circuit. The Ba target was prepared by dissolving BaCl_2 in DI water ($20\ \text{g}/100\ \text{mL}$). $2\ \text{mL}$ was used as the liquid target.

3.3.1.3 Post-target-manufacture testing

Apostolidis *et al.* monitored targets for radon emanation and “standard helium diffusion testing (*UL500, Leybold*).” [18] To ensure leak-tightness, targets were also heated in solution of $0.1\ \text{M HCl}$ at $100\ ^\circ\text{C}$ for 1 h.

3.3.1.4 Holder Assemblies

Apostolidis *et al.* [18] describe a schematic outlining the set-up and holder for the silver-foil prepared targets for proton irradiation, and is replicated in Figure 4.

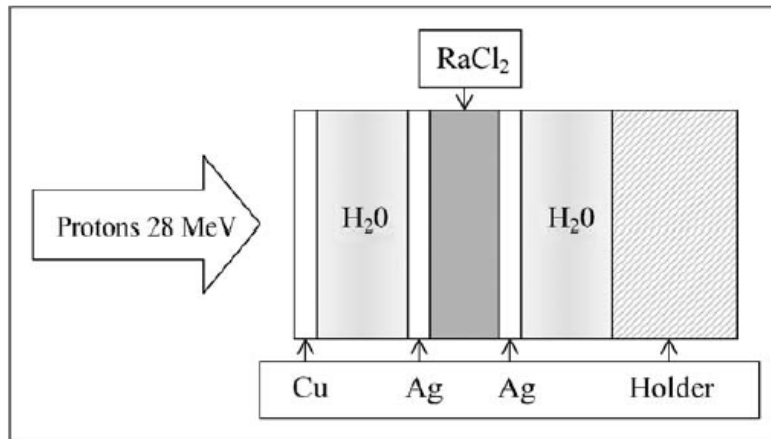


Figure 4 Schematic view of the target design used for proton irradiation of radium chloride. Figure taken from reference [18]

The target box assembly to utilise Nagatsu et al [20]'s electrodeposited target is shown in Figure 3, where ^{226}Ra was electrodeposited on the conical shaped pressed body.

Patent WO1999063550A1 [21] shows an irradiation target assembly to mount a silver capsule surrounded by a cooling circuit. This is illustrated in Figure 5. There is a window in the wall of the casing.

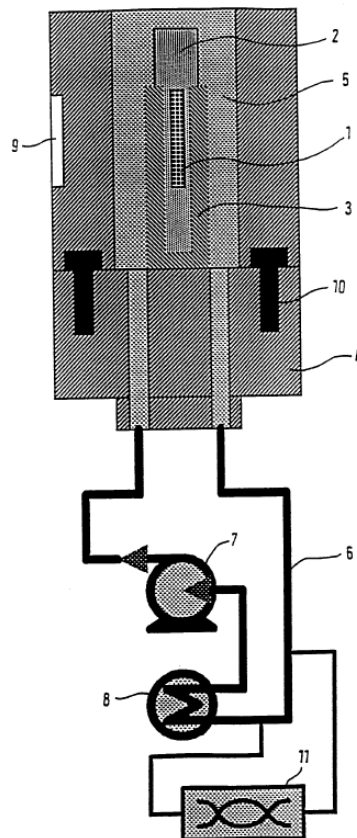


Figure 5. ^{226}Ra target assembly prepared to receive a proton beam from cyclotron source used for producing ^{225}Ac with protons [x] (1) target pellets, (2) capsule made of silver, (3) frame-like support, (4) two-part casing, (5) not defined in patent, (6) outer water cooling circuit, (7) circulation pump, (8) heat exchanger, (9) window, (10) screws, (11) alpha monitor. Image taken from WO1999063550A1 [21].

3.3.1.5 Yields

Apostolidis et al [18] demonstrated mCi yields of ^{227}Ac from mg quantities of ^{226}Ra , and these are tabulated in Table 4.

Table 4. mCi of ^{227}Ac yields from mg quantities of ^{226}Ra , as shown by Apostolidis et al [18]

Irradiation parameters and reaction yields of proton irradiation of Ra-226 targets				
Mass of Ra-226 (mg)	12.5e-3	30.0	30.5	30.1
Proton current (μA)	10	25/50	20	50
Incident proton energy (MeV)	16.8	16.0	16.0	15.9
Target surface (mm^2)	36	200	200	200
Irradiation time (h)	7	49.3	26.3	45.3
Ac-225/Ra-226 (% activity)	16.6	12.5	18.7	43.5
Ac-225 produced (mCi)	2.1e-3	3.8	5.7	13.1

Also described was a proposed 24 hour irradiation of 50 mg ^{226}Ra , if irradiated at 15-16 (maximum excitation function) with a current of 100 mA protons, the expectation is to yield ~ 5 GBq ^{225}Ac , which would be equivalent to 500 patient doses of 10 MBq ^{225}Ac . [19]

After irradiation of 30 mg of ^{226}Ra with 100 μA of protons for 24 hours, 5 GBq of ^{225}Ac was produced, about 1/3 the calculated maximum thick-target yield. [19]

Using electrodeposited targets Nagatsu *et al* [20] obtained ^{225}Ac at a yield of 522–2430 kBq (14–66 μCi , decay corrected) from a ^{226}Ra target of 13.5–37.5 MBq (366–1010 μCi) irradiated by 20 μA protons for 3–5 h.

Patent EP3800648A1 [23] describes a method for producing both ^{212}Pb and ^{225}Ac from a ^{226}Ra target. "The Ra-226 containing target comprises any of RaCl_2 , $\text{Ra}(\text{NO}_3)_2$, $\text{Ra}(\text{OH})_2$ or RaCO_3 . It is an advantage of embodiments of the present invention that different types of Ra-226 containing targets can be used." A stacked target assembly is proposed, for a co-production of ^{225}Ac and ^{212}Pb . Examples given include, for an assembly illustrated in Figure 6. "an entrance beam energy of 25 MeV, a target of (1.51 - 0.793) 0.717 g/cm² is placed in the beam as the first target, where the beam exits this target at 17 MeV. Next, a target of (0.793 - 0.332) 0.461 g/cm² is stacked directly behind it, where the beam exits at 10 MeV. This way, optimization of isotope production was obtained".

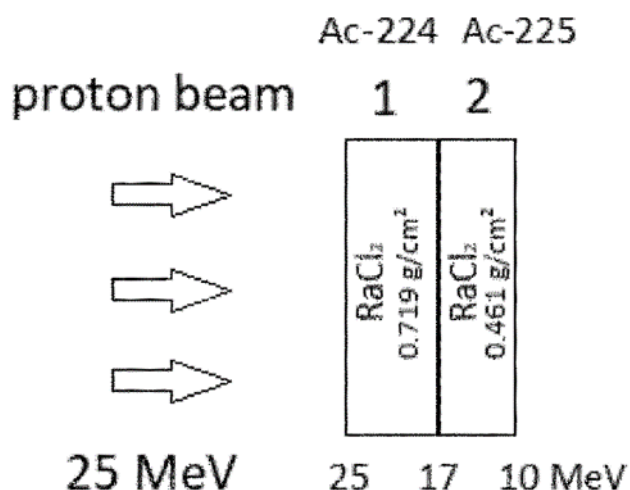


Figure 6. Proposed stacked assembly of ^{226}Ra targets outlined in patent EP3800648A1 [23]

Patent number US8349391B2 [24] describes a method to create a target for production of radionuclides by irradiation with accelerated protons, by deposition of radium via evaporation. The radium salt is proposed to be evaporated on a surface of an aluminium cup to produce thicker targets than those able to be prepared by electrodeposition. The radium is

evaporated from a radium-salt containing aqueous-organic solution or suspension. Radium salts particularly mentioned include “nitrate, carbonate, chloride or oxide and/or mixtures thereof. Nitrate has proved to be particularly suitable”. Layers of radium can also be deposited sequentially to produce desired thicknesses. Figure 7 shows a cut-away view of this cup-shaped radium target.

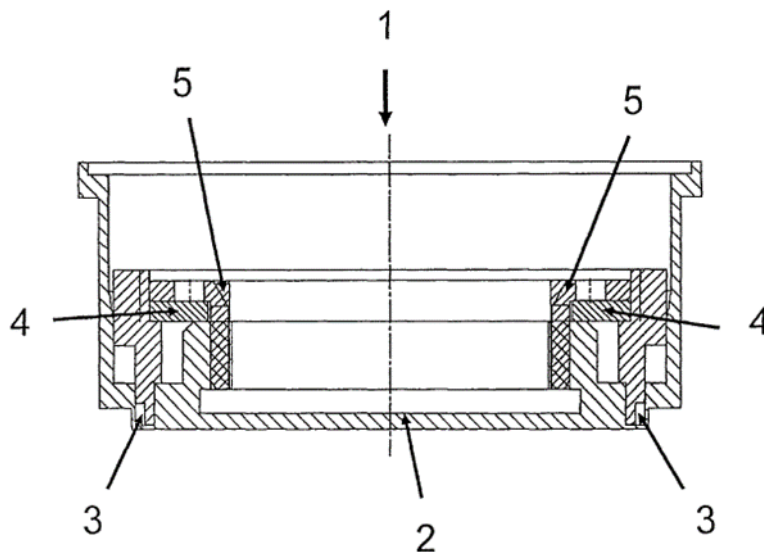


Figure 7. Cross-sectional view of a cup-shaped radium target according to patent number US8349391B2 [24]. (1) target cup, (2) base, (3) groove shaped recess, (4) seal, (5) integrated centrepiece.

The sample holder described in Patent number US8349391B2 [24] is described to be gas-tight and water-tight, via an o-ring, stepped ring and centrepiece. The target is water cooled during irradiation.

3.3.2 Method 2b: $^{232}\text{Th}(p,4n)^{229}\text{Pa}$

The method based on proton irradiation of thorium-232 to obtain actinium-225 was studied by Justin Reed Griswold [25]. The effective cross section and yield measurements for large-scale production of ^{225}Ac through the high-energy proton bombardment of ^{232}Th were reported.

Targets irradiated at IPF were composed of arc-melted thorium metal that was rolled to the thickness of the finished target and trimmed to its final dimensions. X-ray fluorescence spectroscopy of the thorium stock confirmed a composition $\geq 99.6\%$. These thorium discs were electron-beam welded into machined Inconel capsules (Figure 8). During irradiations at IPF, instantaneous beam intensities were monitored and logged at one and ten second intervals by two inductive current monitors. In the past, recorded beam histories have been compared with integrated fluences measured by established monitor reactions and found to be accurate within 5%.

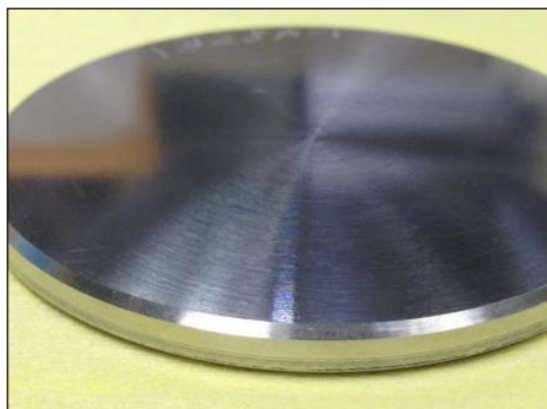


Figure 8. Inconel-encapsulated thorium disk before irradiation at IPF

After irradiation, targets were allowed to decay at IPF to U.S. Department of Transportation (DOT) Type A quantities and then moved to the processing facility where the Inconel encapsulation was cut open. The irradiated thorium was then removed from the Inconel cladding, repackaged in a glass vial, and shipped to ORNL for chemical processing.

However, simulated cross sections for the $^{232}\text{Th}[p,x]\text{Ac}$ reactions consistently differed from the experimental data by a factor of two. As documented, curie quantities of ^{225}Ac can be produced in a ten-day irradiation of a 5 g cm⁻² thorium target at either LANL-IPF or BNL-BLIP at proton energies between 77 and 192 MeV and proton intensities from 100 to 250 μA . The first in-depth study of the long-lived radiocontaminants of $^{225}\text{Ac}/^{213}\text{Bi}$ generators produced through the high-energy proton irradiation of ^{232}Th has been performed. After thorough analysis of the bismuth fraction eluted from the generator by a method commonly used in the nuclear medicine field, no unknown radiocontaminants were observed. Only a small fraction of breakthrough ^{227}Ac and its decay products were present. Similar results were obtained through the 6 M HNO_3 elution of the generator; revealing only ^{227}Ac and ^{227}Th . Mass spectrometry analysis on future $^{225}\text{Ac}/^{213}\text{Bi}$ generators could reveal the presence of unknown contaminants, but this analysis may only confirm the efficiency of the current ^{225}Ac purification scheme employed at ORNL. Results achieved with the physical models used in PHITS can be compared to an equivalent MCNP or GEANT4 analysis, further validating the efficacy of these useful simulation tools. In addition, a radioactive decay and target burnup component could be added to PHITS to allow for a more accurate comparison with the effective cross-sections measured in these experiments.

Although easily separable from ^{225}Ac through ion exchange chromatography, ^{233}Pa is one of the highest activity contaminants produced in the high-energy proton irradiation of ^{232}Th and can cause shipping limitations. The exact nuclear reaction pathway that produces this radionuclide is currently unknown but two possible pathways include the $^{232}\text{Th}[p,\gamma]^{233}\text{Pa}$ reaction or the $^{232}\text{Th}[n,\gamma]^{233}\text{Th}(\beta^-)\rightarrow^{233}\text{Pa}$. However, both of these pathways are unlikely at high incident proton energies. If a small thorium foil were irradiated behind a thicker thorium foil and a higher specific activity of ^{233}Pa was observed in the smaller foil, a case could be made that the main nuclear pathway for the production of ^{233}Pa is through the absorption of secondary neutrons.

3.3.3 Method 2c: $^{230}\text{Th}(p,2n)^{229}\text{Pa}$

At this current time, this method has been only theoretically proposed, so no target requirements/materials can be extrapolated from the literature.

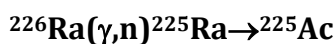
3.4 Method 3 – Deuteron Irradiation (d,3n)

$^{226}\text{Ra}(d,3n)^{225}\text{Ac}$

A route for deuteron irradiation of ^{226}Ra to produce ^{225}Ac via $^{226}\text{Ra}(d,3n)^{225}\text{Ac}$ is proposed by Morgenstern *et al.* [26] and also explored in patent no. WO2004079751A2. [27]

Targets contain radium as RaCl_2 , formed by precipitation from concentrated HCl . The RaCl_2 was heated to release crystal water (150-200 °C) and pressed into a pellet. The pellet was enclosed in a metal envelope (Ag, Ti or Nb), chosen for the insolubility in HCl and high thermal conductivity. Nb, additionally, is less activated by the reaction than Ag or Ti. The envelope was sealed within an aluminium capsule. The pressure build-up within the capsule is minimised by the elimination of the crystal water in the pre-pelletisation step. Cross sections have not yet been measured experimentally, but models predict a maximum cross-section of 864 mb at 18.5. [26] This proposed route is likely to produce an increase in unwanted isotopes, such as ^{226}Ac (via $^{226}\text{Ra}(d,2n)^{226}\text{Ac}$) compared to the (p,2n) method 2 route.

3.5 Method 4 – Gamma Irradiation (γ, n)



^{225}Ac can be produced from a target of ^{226}Ra by the photonuclear reaction, $^{226}\text{Ra}(\gamma, n)^{225}\text{Ra}$ where ^{225}Ra ($T_{1/2} = 14.9$ d) decays via beta-decay to ^{225}Ac . Photons can be produced by electrons of about 25–30 MeV. It has been calculated that it is possible to produce about 148 GBq (4 Ci) of ^{225}Ra from a 10-day irradiation of a 1 g radium target at 25 MeV and 20 kW of electron beam power. If milked three times over a 45-day period, this target would yield about 148 GBq (4 Ci) of ^{225}Ac . [28] The reaction is described as having a photon energy threshold of 6.4 MeV, although experimentally measured cross-section data are not available to date (2019) [29].

Maslov *et al* [30] irradiated two thin targets each containing 0.65 μg of ^{226}Ra . One target contained a mixture of powdered barium sulphate and radium sulphate, the other consisted of radium nitrate on an aluminium support. Each target was placed in a cylindrical aluminium container 8 mm in diameter and 5 mm high. The container was closed with an aluminium lid 0.1 mm thick. The container was fixed at the centre of an aluminium holder open on one side. The open side of the holder was tightly sealed with 50- μm aluminium foil. The targets were irradiated on an MT-25 microtron for 30 and 20 h with photons having the maximal energy of 24 MeV at the electron current of 24 MeV. The radiation yield of ^{225}Ac was 550 Bq/ $(\mu\text{A h mg } ^{226}\text{Ra})$.

Diamond and Ross illustrate an example of a high-power radium target used for electron irradiation. This is reproduced in Figure 9. Two sections of high-purity aluminium metal encapsulate the radium, which has been previously heated to reduce moisture content. The aluminium cladding of the base has a reservoir channel to account for the helium that is produced by the alpha decay, both during irradiation, and post-irradiation. The aluminium is sufficiently thick to withstand the expected pressure increase.

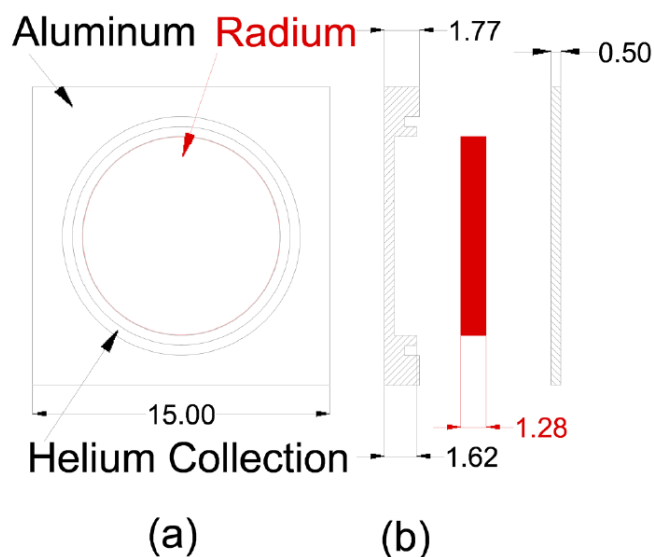


Figure 9. Example of a high-powered radium target for electron irradiation; a) shows a top view of the target and b) shows the details of the three sections of the target assembly. Dimensions are in mm.

Diamond and Ross [28] also show an example of a target chamber, modelled on the high-power neutron target used at the Oak Ridge Electron Linear Accelerator (ORELA) neutron source. [31] The target chamber schematic is reproduced in Figure 10, and shows a target chamber that can hold two radium targets, such as those shown in Figure 9.

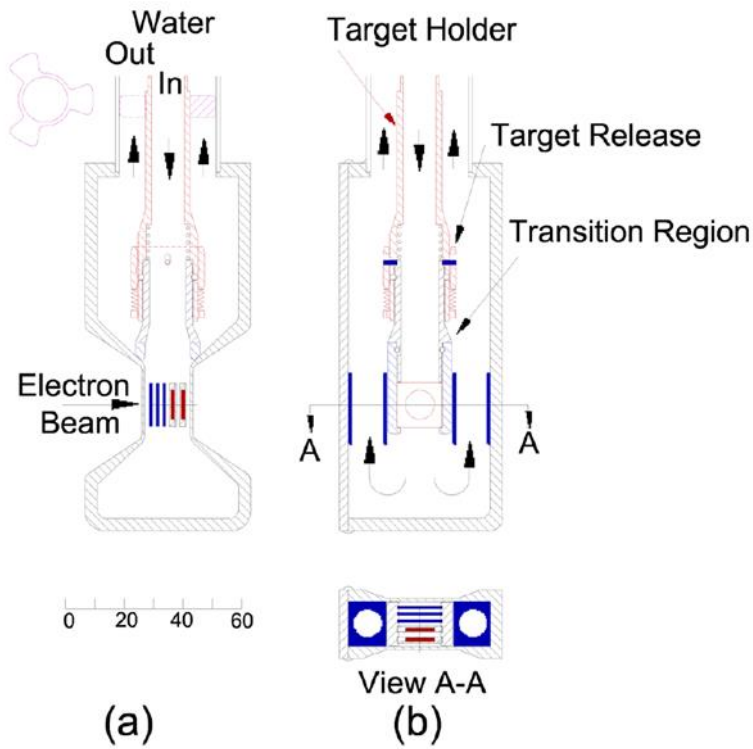


Figure 10. Example of a high-power target chamber that contains both an optimized converter target and an assembly of two-radium targets for electron irradiation, (a) shows the electron beam, the window, and targets and (b) shows the view at 90°. View A-A shows the water passages for the return water flow. Dimensions are in mm. Figure taken from reference [28]

The aluminium target chamber, as shown in Figure 10, uses three one-millimetre tantalum plates with gaps for water cooling, alongside two radium targets. Tantalum was chosen due to tantalum isotopes produced (^{180}Ta and ^{178}Ta) having short half lives and will be significantly decayed once processed, and other isotopes being produced are not expected to be additionally challenging to handle. Compared to proton irradiation, thicker encapsulation material can be used.

Diamond and Ross [28] also outline a target configuration that could be adopted to use radium salts in fine-powder form with the basic configuration outlined in Figure 9, modified to produce channels to provide additional cooling. The proposed target/holder is shown in Figure 11.

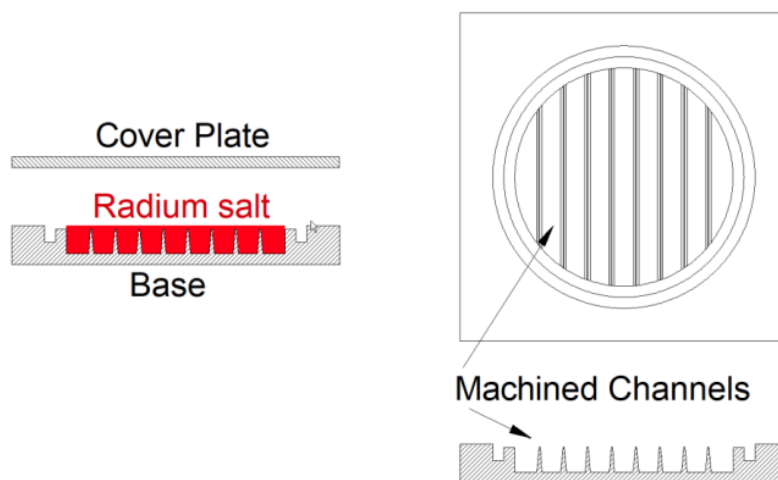


Figure 11. Radium target with machined channels designed for irradiations of powdered radium salts. Figure taken from reference [28].

Commercial company Niowave (Lansing, Michigan) produces ^{225}Ac in electron linac using liquid ^{226}Ra targets [32]. The radium target is a liquid (nitrate) solution, which provides for target cooling by circulation and allows a continuous extraction. ^{225}Ac is extracted from the target solution containing both target and product isotopes by radiochemical separation. Up to 100 g of ^{226}Ra is proposed to be used in the liquid target in the final configuration.

Authors of the patent [33] propose solid and liquid ^{226}Ra targets for production of ^{225}Ac in an accelerator. According to the authors proposed invention provides a reliable method for obtaining greater than 1000-millicurie quantities of $^{225}\text{Ac}/^{213}\text{Bi}$ in $<5\text{-}\mu\text{Ci } ^{225}\text{Ra}/100 \mu\text{Ci } ^{225}\text{Ac}$ radionuclide purity via bombardment of ^{226}Ra .

The ^{226}Ra target is formed by electroplating, which forms radium dioxide upon exposure to air. The base converting material (0.5 mm - 1.7 mm thick) is proposed to be comprised of copper, tungsten, platinum and/or tantalum, and may be electroplated with nickel before radium. The concentration of radium is described as *“about 80 mg/cm² to about 160 mg/cm².”* The electron beam current used is described as *from about 100 microampere to about 1000 microampere* with electron energies *“from about 20 MeV to about 25 MeV”* and photo energy *“of from about 10 MeV to about 25 MeV”*. An alternative route also proposed within this patent towards creating a radium-containing targets, is via radium bromide or oxide mixed into a varnish and painted onto the converting material. Patent US6680993 B2 [33] also proposes a liquid ^{226}Ra target in the form of 0.5-1.5 molar radium chloride. This is proposed either to flow over the converting material or contained in a quartz vial.

3.6 Reactor Target Summary

For reactor irradiation, for example in the HFR in Petten, materials are predominantly irradiated in solid form as powder or compact disks or cylinders. Target materials in powder form can be contained in quartz ampules and put in an aluminium- or HDPE-containers. Quartz ampules need to be of sufficient size to fit the powder material and be sealed. In addition, an insert can be used to keep the ampule or target material in place which is always made from aluminium or graphite. Both aluminium and graphite are transparent to neutrons and easy to come by manufacturing materials. However, graphite itself does get activated to a certain extent. An added benefit of graphite is that lends itself as an easy material to drill holes in in which target discs can be immobilized. In this way, it is easy to drill multiple holes in a solid graphite cylinder and immobilize a large number small targets in a graphite grid inside one small aluminium container.

Dry and unreactive target materials are preferred as chemical reactions during irradiation are unwanted, especially reactions with water. Dissociation of the target material is also unwanted as this causes pressure build-up. Too large pressure build-ups can break the quartz ampule and should always be avoided. During irradiation, the temperature in the ampule or container is kept below the melting point of the target material. This can be done by choosing a material with a high melting point, but this can also be done by proper cooling of the target channel in the irradiation facility. The latter is taken into account in the design of the outer aluminium container.

Furthermore, impurities need to be kept as low as possible. Some isotopes give considerable issues after irradiation. Co-60 is an unwanted by-product as it has a long decay time of 5.3 years. Na-24 is also problematic as it produces high energy gamma radiation and even a decay half-life of 14 hours is very problematic if radionuclides are produced that need to be quickly transported to patients. It requires a lot of cooling time after irradiation to lower the dose rate to safe levels for handling and transport.

3.7 Method 5 – Neutron Irradiation

3.7.1 Method 5a: Thermal Neutron (n, γ)

Oak Ridge National Laboratory (ORNL) has communicated intention to irradiate ^{226}Ra pellets in their HFIR. The radium target is in a carbonate form, within an aluminium mixture, sealed within an aluminium liner. The proposed pellet schematic is shown in Figure 12. The aluminium liner is seamless and uses aluminium powder caps to press and seal the radium carbonate.

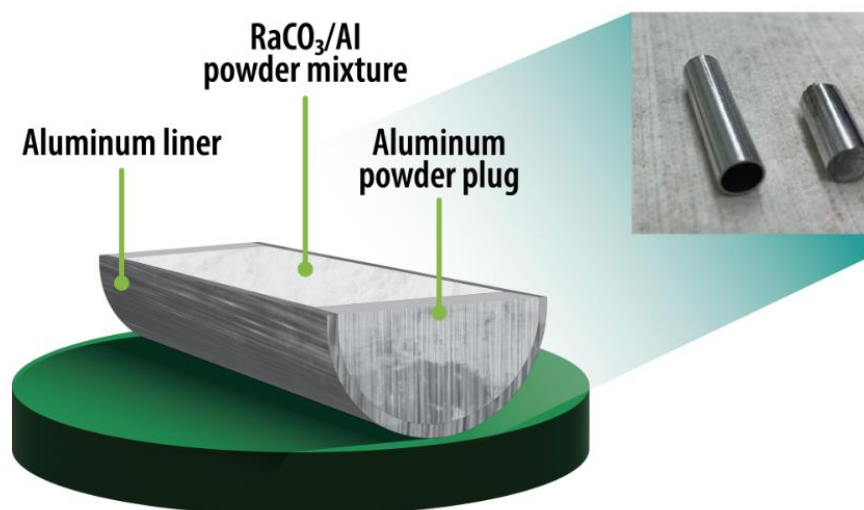


Figure 12. An illustration shows how the composite is pressed into a seamless aluminium liner, which is then sealed with an aluminium powder cap. Illustration taken from ORNL webpage [34]

ORNL have also proposed a HFIR irradiation of a ^{226}Ra target to produce ^{229}Th . [35] In this experiment the target was $43.5\ \mu\text{g}$ ^{226}Ra in nitrate form. The quoted yield was ^{229}Th is $31\ \mu\text{Ci}$ per mg of ^{226}Ra per reactor cycle. Within this irradiation, significant quantities of ^{228}Th and ^{227}Ac contaminants were co-produced. It is suggested that recycling of the ^{226}Ra target could result in an increase in yield of ^{229}Th due to formation of ^{228}Ra .

3.7.2 Method 5b: Fast Neutron (n,2n)

A fast neutron production method for ^{225}Ac has been theoretically proposed by researchers at the experimental fast reactor Joyo, which is owned and operated by Japan Atomic Energy Agency [36], however limited details of the proposed target geometry are given. A mention is given to “a large loading region with high heat removal capacity” [37]. It was proposed that the theoretical analysis shows that $47\ \text{GBq}$ of ^{225}Ac could be generated annually by irradiating $1\ \text{g}$ of ^{226}Ra . Alternatively it was proposed that by irradiation of $50\ \text{g}$ of ^{230}Th , $6.5\ \text{GBq}$ of ^{225}Ac could be semi-permanently generated every year.

Patent EP0752710A1 [38] outlines a process of producing ^{225}Ac from a ^{226}Ra target via a “fast” reactor with high energy neutrons (originating from a spallation source), however no target descriptions are given.

US20140226774A1 [39] describes an “actinium-227 production device”, which although is not for the production of ^{225}Ac , describes a thermal-neutron shielding method, geometry and materials suitable for the irradiation of ^{226}Ra targets. It is envisaged that actinium-227 can be milked for recovery of radium-223. The other radioisotope envisaged to be produced by this

method is thorium-228. This patent describes a device to create a tailored neutron spectrum to suppress production of less desirable radioisotopes being formed under irradiation. It describes target forms and containment with thermal-neutron shielding effects which envisage the neutrons reaching the target material are in the range of 20 eV to 1 KeV. The target device is designed to irradiate compacted ^{226}Ra in its carbonate form. Particles of radium carbonate are used due to the presence of voids, which allow volume to contain the ^4He generated by the ^{226}Ra decay. Additional “plenum” volume is provided by the geometry of the caplet (hexagonal, octagonal, square, rectangular or trapezoidal) surrounding the disk of compacted material. If self-shielding effects are required, the density can be increased by addition of metallic ^{226}Ra beads in the central region of the target.

In addition to the tailored neutron spectrum, the sealed capsule design is also described. Due to the first decay daughter of ^{226}Ra being ^{222}Rn , the capsule is designed to be “radon tight”. In this invention, the irradiation time is proposed to be 5-10 weeks, and the radon is envisaged to be contained. The described caplet containments are “small, hollow, finely machined metal disks fitted together and welded shut”, which qualify as sealed sources. Each caplet contains a compacted ^{226}Ra disk. A stack of sealed caplet is enclosed in a set of nested cylinders, with each cylinder also being welded shut. Suggested materials for the encapsulation materials are: “aluminum alloy (aluminum-6061), zirconium alloy (zircalloy), qualified stainless steel alloys (HT-9, SS-316) or titanium alloys as well as other alloys used for sealed sources”. The assembly material can also contain strong thermal neutron absorbers to capture thermal neutrons. Suggested neutron absorbers are erbium or europium in oxide form or metallic foil form. Intermetallic hydrides or deuterides can also be incorporated to slow fast neutrons to the desired (epithermal) energy range. These modifications can increase the efficiency of the method of production. The patent also references Patent number 3269915 (1966) which describes neutron absorbing materials such as cadmium, samarium and/or gadolinium to influence the neutron spectrum. Radon-absorbing materials such as silver exchanged zeolite and activated charcoal are proposed to be contained within the target enclosure. A proposed target assembly containing eight ^{226}Ra carbonate caplets is shown in Figure 13.

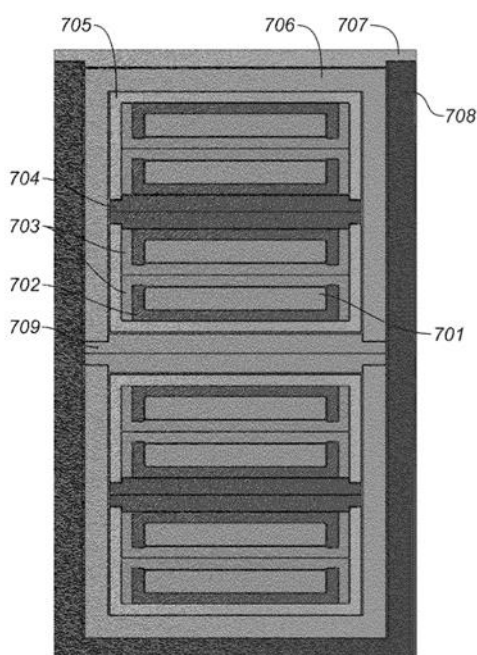


Figure 13 taken from patent no. US20140226774A1. [39] A cross-sectional view of an array a target assembly of eight ^{226}Ra carbonate caplets. The cut-away shows the (701) ^{226}Ra carbonate, (702) caplet cups, (703) caplet lids, (705) pair cup, (704) pair cup lid, enclosed by (706) two pair cup, (709) two pair lid, (708) exterior can and (707) exterior lid.

4 QUALITY/PURITY OF ²²⁶Ra TARGET MATERIALS

4.1 Purity

Very high chemical purity is mandatory to minimize coproduction of disturbing radionuclides by activation of chemical impurities. However, the allowable limits differ widely for different chemical elements. In particular elements with high neutron capture cross-sections and/or those leading to longer-lived radionuclides such as Sc, Co, Ag, In, Cs, Sm, Eu, Tb, Hf, Ta, Os, Au, U are critical. Depending on the cross-sections of the main target material such impurities can lead to noticeable radionuclidic impurities, even when present at the level of ppm. Moreover, the presence of Na, Ga, Br or La will lead to radionuclides Na-24, Ga-72, Br-82, La-140 emitting hard γ -rays that may dominate the overall dose rate of an irradiated target outside a heavy metal shielding. Whenever an irradiated target needs to be shipped rapidly before these short-lived activities have decayed it is advisable to minimize such chemical impurities.

4.1.1 ²²⁶Ra Legacy Source Purity

From its discovery in 1898 ²²⁶Ra was used in a range of products including toothpaste, hair cream, bath tonics and clock faces. Once the effects of radiation were better understood its use was regulated and limited to medical applications and industrial use, such as instrument calibration, oil well logging and soil logging devices. Historic ²²⁶Ra material presents a waste storage issue due to its long half-life ($T_{1/2} = 1600$ y), its daughter isotope ²²²Rn (radon gas) and He gas accumulation in containment (through four alpha decays per ²²⁶Ra decay). These sources have typically been collected through safeguards initiatives and are held within long-term storage facilities. This will be further discussed in D1.2 and/or D1.9.

Encapsulation of ²²⁶Ra within seed/ capsules, or needles for treatment for cancer tumours was commonplace within the early 20th century. These devices were filled with radium salt powders (typically radium sulphate) and an inert filler (e.g. zirconium chloride), typical contents of which can be found in Table 5. Successful extraction of ²²⁶Ra from used brachytherapy needles has been demonstrated previously through dissolution in a solution of HCl and HNO₃, the Pt/Ir needles were heated in the solution under reflux until the cap ends dissolved and the salt released into solution. The Ra containing solution was then filtered and passed through a cation-exchange column and washed with HCl. ²²⁶Ra can then be eluted using HNO₃ for target preparation [5].

Table 5. Legacy sources of ²²⁶Ra with radionuclides present and expected contaminants.

Source material	Radioisotopes present	Other contaminants	References
Brachytherapy needles	²²⁶ Ra, ²¹⁰ Pb, ²¹⁴ Pb, ²¹⁴ Bi, ²²² Rn	Sulphate, bromide, zirconium chloride, gold, silver, platinum, iridium, barium	Nagatsu [20], Melville [40], Hogle [5], Kemikler [41], Maddock [42], Quafmolla [43]
Ra-Be sources	²²⁶ Ra, ²²⁷ Ra, ²²⁷ Ac, ²¹⁰ Pb, ²¹⁴ Pb, ²¹⁴ Bi, mesothorium (²²⁸ Ra)	Beryllium, fluorine, carbon	Didi [44], Elish [45], Soderquist [12], Bak [46]
(TE)NORM waste	²²⁶ Ra, ²³⁰ Th, ²²² Rn, ²¹⁰ Pb, ²¹⁴ Pb, ²¹⁰ Po, ²³⁸ U, ²³⁵ U	Soil and other geological material, barium, lead	Hutchingson [47], Roessler [48], Iyengar [49], Leopold [50], Al Abdullah [51], Siddeeg [52], Carvalho [53], Averill [54], Landsberger [55], Chautard [56]
Industrial and consumer products	²²⁶ Ra, ²²² Rn	Metal products, zinc sulphide, beryllium and carbon (if neutron gauges)	Gilmore [57], Pratt [58], Quafmolla [43], Martland [59], Robinson [60]

Finely divided, mixed powders of radium and beryllium (Ra-Be) are used within sources with a wide range of application in industry; these can be used for analytical and monitoring purposes, such as in moisture, porosity and sensitivity gauges, or used as a neutron source [45] [44] [12]. Some small reactors require an intrinsic neutron source to initiate a neutron

flux. These 'start-up' sources typically consist of an alpha emitting radionuclide combined with beryllium to provide a supply of fast neutrons through and (α,n) reaction. The absorption of an alpha particle by ^9Be leads to the formation of ^{12}C with the release of a neutron. Some start-up sources were manufactures using ^{226}Ra as the alpha emitting material, but have since typically been replaced by those with $^{241}\text{Am}/\text{Be}$ (α,n) or ^{252}Cf (spontaneous fission).

Many industries which make use of processing earths geological materials to create products (e.g. mining ore, hydrocarbon extraction) result in the concentration of naturally occurring radioactive material (NORM), an example of which is the accumulation of ^{226}Ra through uranium mining. Typical activities of ^{226}Ra reported should be considered alongside the specific activity of ^{226}Ra , as such in mass terms these concentrations typically fall within ppt range.

4.2 Chemical Form

Chemical forms that have been considered at NRG for the production of ^{226}Ra targets are the oxide, carbonate and the nitrate form.

Oxides:

Oxides are the preferred form for the minimization of potential pressure build-up assuming complete dissociation of the material during irradiation. However, radium oxide is not straight-forward to synthesise or handle. Synthesis would most likely require decomposition of either the carbonate, nitrate or hydroxide salt at high temperatures. Furthermore, RaO is presumed to be hygroscopic which makes storing and handling challenging. Since RaO reacts with water to form $\text{Ra}(\text{OH})_2$, transferring RaO to an ampule by means of dissolving and pipetting is, as far as we know, not practically possible.

Nitrates:

Nitrates would produce more pressure build-up compared to oxides when completely decomposed during irradiation. However, currently, it is the preferred chemical form for target manufacturing as radium nitrates are highly soluble. This eases the method for dispensing the radium nitrate batch solution into different targets.

Carbonates:

Carbonates were considered as dissociation of the material requires higher temperatures than nitrates. However, carbonates are much more difficult to dissolve for post irradiation processing. Therefore, this chemical composition was not chosen.

Barium issues:

Typical ^{226}Ra material is obtained from brachytherapy needles that also contain a large amount of barium. It is likely that this barium was added to increase the volume for handling as the tiny amounts of radium needed for brachy therapy needles were difficult to handle on their own.

Unfortunately, having barium, and/or other cationic impurities like calcium or sodium in the target material, will result additional nitrate salts deposited in the target material, even after evaporation of the solvent. The larger quantity of nitrates in the target material will increase the pressure build-up from decomposition of the target material during irradiation. Radium salts such as radium chloride can be used, but the material introduced by using a salt may have impact of the yield. Radium nitrate, radium carbonate, and radium sulphate produce short half-life products such as ^{13}N ($T_{1/2} = 10$ min) and ^{15}O ($T_{1/2} = 122$ s) for radium nitrate and ^{11}C ($T_{1/2} = 20.4$ min) and ^{15}O ($T_{1/2} = 122$ s) for radium carbonate. [28]

4.2.1 Purity requirements/Chemical form

4.2.1.1 Pre-Irradiation

Apostolidis [18] used a source material (RaCO_3) containing ^{227}Ac contamination. This was purified before use using selective evaporation/dissolution procedures and chromatographic resin. The radium-containing stock solution was analysed by ICP-MS for ^{227}Ac contamination.

Nagatsu *et al.* prepared a ^{226}Ra target by electrodeposition. [20] The radium was obtained from legacy Ra sources (radium needles). After several extraction and separation steps, from an initial assumed RaSO_4 -form, the radium was yielded in hydroxide form. This was not further (chemically) purified.

4.2.1.2 Post-irradiation

Apostolidis [18] et al reported post-irradiation by-products ^{226}Ac ($T_{1/2} = 29$ h) and ^{224}Ac ($T_{1/2} = 2.9$ h) through $^{226}\text{Ra}(p,n)^{226}\text{Ac}$ and $^{226}\text{Ra}(p,3n)^{224}\text{Ac}$ reactions were “negligible with respect to the isotopic purity of the actinium product.” Once the actinium was purified, the ^{226}Ac was below the limit of detection. Ra/Ac separations removed ^{224}Ra (formed from ^{224}Ac) and ^{225}Ra (formed via $^{226}\text{Ra}(p,pn)^{225}\text{Ra}$). It is stated by Morgenstern *et al.* that impurities of the short-lived ^{226}Ac and ^{224}Ac “can be minimized through selection of appropriate proton energies”. [19]. Unwanted short-lived isotope activity can also be minimised with considerations towards cooling and processing times.

Purity after extraction chromatography can be measured using alpha and gamma spectroscopy and compared against material obtained from legacy ^{229}Th material. [18]

Initial published studies indicate that the impact of the ^{227}Ac impurity on patient dosimetry “will be negligible”, [61] however, long-lived ^{227}Ac impurities may lead to complications hospital and clinical settings related to licensing and waste disposal as well as considerations of safe handling techniques.

Nagatsu et al [20] used alpha spectrometry with an acquisition time of 1200 s to measure other isotopes present in aliquots of irradiated samples. These are tabulated in Figure 14.

Run	#1	#2	#3
Beam condition ($E_p = 15.6$ MeV)	20 $\mu\text{A} \times 3$ h	20 $\mu\text{A} \times 5$ h	20 $\mu\text{A} \times 5$ h
Ra deposition			
^{226}Ra , initial electrolyte	14.5 MBq (391 μCi)	36.4 MBq (984 μCi)	38.8 MBq (1.05 mCi)
^{226}Ra , deposited	13.5 MBq (366 μCi)	35.4 MBq (956 μCi)	37.5 MBq (1.01 mCi)
Deposition rate (%)	94	97	97
Nuclides of interest* in the initially purified sample (kBq, decay corrected to EOB)			
^{225}Ac (150 keV, 0.6%)	522	2.23×10^3	2.43×10^3
^{226}Ac (230 keV, 26.9%)	111	451	488
^{224}Ac (215 keV, 52.3%)	Not detected	Not detected	Not detected
^{226}Ra (186 keV, 3.64%)	Not detected	Not detected	Not detected
^{214}Pb (352 keV, 35.6%)	Not detected	Not detected	Not detected
^{214}Bi (609 keV, 45.5%)	5.2	13.5	33.3
^{135}La (481 keV, 1.52%)	84.5	333	344
^{140}La (487 keV, 43.9%)	0.0571	0.165	0.231
^{212}Bi (727 keV, 6.58%)	Trace	Trace	Trace
^{208}Tl (2615 keV, 99.8%)	Trace	Trace	Trace

Figure 14. Table taken from reference [20] tabulating detected isotopes post-irradiation. Nuclear data presented in parenthesis are used for quantification.

Nagatsu et al [20] outline steps to reduce the amount of ^{226}Ac in the final product by cooling the intermediate products for 10 half-lives or more, for 2-3 weeks.

5 CHALLENGES OF ²²⁶Ra AS A TARGET MATERIAL

Infrastructure and handling of ²²⁶Ra will be covered in more detail in D1.2.

Radium is a highly radiotoxic element. It is situated in group II of the periodic table and is heaviest alkaline metal in this group. It is a highly reactive metal that has poor physical, chemical, and thermal properties for the use as a target material. The safe handling of radium, the management of radon emanation, and the gas-tight containment of helium gas build-up are currently the main challenges towards target preparation and routine radionuclide production.

The poor thermal properties of radium limit the maximum power density that can be applied. Thermal properties include: [28]

thermal conductivity of 19 W/m · K,

melting point of 963 K

specific heat of 0.12 kJ/kg K.

²²⁶Ra is part of the decay chain of ²³⁸U. As illustrated in Figure 15, ²²⁶Ra decays by alpha emission to ²²²Rn, a noble gas with a half-life of 3.6 days. Before the decay chain ends with the stable isotope ²⁰⁶Pb it has generated a further eight radionuclides of which four are alpha emitters. Each decaying ²²⁶Ra atom thus gives rise to five alpha particles. During the decay many high as well as low energy gamma photons and beta particles are also emitted. In a radium source these daughter radionuclides are also present, which contributes to the definition of 'a high dose factor'.

Radium is an alkali earth metal. It is very reactive and reacts even with nitrogen. In radioactive sources radium is therefore always used in the form of salts, which may be bromide, chloride, sulphate or carbonate. All are soluble in water in amounts which can give rise to radiological problems. These salts may be dispersed as powder if the source encapsulation is damaged. *In-vivo*, radium shows analogous behaviour to calcium, binding to hydroxyapatite, leading to a potential concentration effect in the bone, where it has a significant biological half-life. Stored radium should be ventilated to prevent build-up of radon.

Radioactive Properties of Radium 226 and its Daughters							
Isotope	Half-Life	Natural Abundance (%)	Specific Activity (Ci/g)	Decay Mode	Radiation Energy (MeV)		
					Alpha (α)	Beta (β)	Gamma (γ)
Ra-226	1600 yr	>99	1.0	α	4.8	0.036	0.0067
Rn-222	3.8 days	-	160,000	α	5.5	<	<
Po-218	3.1 min	-	290 million	α	6	<	<
Pb-214	27 min	-	33 million	β	-	0.29	0.25
Bi-214	20 min	-	45 million	β	-	0.66	1.5
Po-214	0.00016 sec	-	330 trillion	α	7.7	<	<
Pb-210	22 yr	-	77	β	-	0.038	0.0048
Bi-210	5.0 days	-	130,000	β	-	0.39	-
Po-210	140 days	-	4500	α	5.3	<	<

Table 6. Radioactive properties of ²²⁶Ra and its daughters. [Table adapted from EPA online document "Radiation Protection" - no longer available online]

Radiotoxicity calculations

As ^{226}Ra has a half-life ($T_{1/2}$) of 1600 years and decays by alpha emission to ^{222}Rn . Considering 40 mg of ^{226}Ra :

Activity or number of disintegrations per second is given by:

$$\begin{aligned} \text{Activity} &= dN/dt = \lambda \times N = (\ln 2 / t_{1/2}) \times N \\ &= (0.698 / 5.05 \times 10^{10} \text{s}) \cdot (6.03 \times 10^{23} / 5650) \\ &= 1.48 \times 10^9 \text{ Bq} \end{aligned}$$

The radiotoxicity of a nuclide is defined by:

$$\begin{aligned} \text{Radiotoxicity} &= \text{Activity} \times \text{Effective Dose Coefficient} \\ &= 1.48 \times 10^9 \text{ Bq} \times 4.7 \times 10^{-6} \text{ Sv} \cdot \text{Bq}^{-1} \\ &= \underline{6.96 \times 10^3 \text{ Sv}} \text{ (very high value)} \end{aligned}$$

^{226}Ra is a difficult material to handle due to safety concerns, *i.e.*, radon (^{222}Rn) emanation and high-energy gamma emission from the descendants. Figure 15. illustrates the decay chain. As illustrated, ^{226}Ra ($T_{1/2} = 1600 \text{ y}$) yields an α -particle and ^{222}Rn ; ^{222}Rn ($T_{1/2} = 3.82 \text{ d}$) yields an α -particle and ^{218}Po ; ^{218}Po ($T_{1/2} = 3.05 \text{ min}$) yields an α -particle and ^{214}Pb ; ^{214}Pb ($T_{1/2} = 26.8 \text{ m}$) yields a β -particle and ^{214}Bi ; ^{214}Bi ($T_{1/2} = 19.7 \text{ min}$) yields a β -particle and ^{214}Po ; ^{214}Po ($T_{1/2} = 0.16 \text{ ms}$) yields an α -particle and ^{210}Pb ; ^{210}Pb ($T_{1/2} = 22 \text{ y}$) yields a β -particle and ^{210}Bi ; ^{210}Bi ($T_{1/2} = 5.0 \text{ d}$) yields a β -particle and ^{210}Po ; ^{210}Po ($T_{1/2} = 138 \text{ d}$) yields an α -particle and ^{206}Pb ; ^{206}Pb is stable.

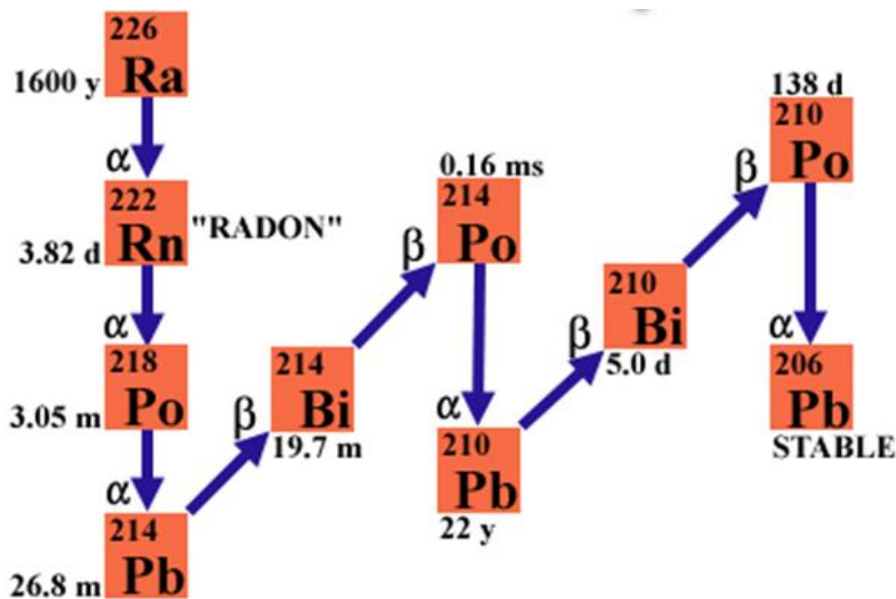


Figure 15. ^{226}Ra decay chain. Figure adapted from NIST website [62]. ^{226}Ra ($T_{1/2} = 1600 \text{ y}$) decays via ^{222}Rn , ^{218}Po , ^{214}Pb , ^{214}Bi , ^{214}Po , ^{210}Pb , ^{210}Bi , ^{210}Po to stable ^{206}Pb .

Directly after a purification step of the ^{226}Ra source material ($T_{1/2} = 1600 \text{ y}$), it takes 14 hours for 10 % of daughters to grow again into the ^{226}Ra material. As such, one should generally consider the dose rate from ^{226}Ra in equilibrium with its daughters and not just the dose rate from pure ^{226}Ra when assessing radiological safety aspects.

^{226}Ra has a similar chemical behaviour to elements like calcium, meaning it accumulates in the bones when ingested. This adds to the hazard of ^{226}Ra as the bones are particularly sensitive to radioactivity. The same accounts for the lungs, which is relevant knowing that the decay product of ^{226}Ra is the radioactive and gaseous ^{222}Rn putting the lungs more at risk when ^{222}Rn is not properly contained.

All of these aspects increase the health risks of working with ^{226}Ra . This means that a limited amount of ^{226}Ra can be handled in a fume hood and that an alpha-tight glovebox is needed to avoid exposure of operators to ^{222}Rn when working with larger amounts of ^{226}Ra . For this reason the e50 values of ^{226}Ra are very small and strict limits and conditions have been imposed by governments for the transport of ^{226}Ra .

5.1 Post Irradiation Purity

During irradiation of ^{226}Ra under a fast neutron spectrum, the undesirable parent nuclide ^{227}Ra of ^{227}Ac emits β^- rays with a relatively long half-life of 21.8 years. In the case of ^{226}Ra irradiation, the major elements produced are radium, actinium, and thorium. After irradiation, the ^{225}Ac must be purified from the Ra and its progeny (e.g. Pb, Po and Bi) before it is to be used. ^{225}Ac is sold by the NIDC [63] in two purity specifications, 'accelerator-produced' with a stated radionuclidic purity of $\geq 99\%$ by activity (gamma spectroscopy), not including ^{227}Ac - or daughter isotopes. The specification gives a value of $\leq 2\%$ ^{227}Ac at shipment (value extrapolated from earlier runs). A 'thorium-229 decay product' is stated with a radionuclidic purity of $>98\%$ ^{225}Ac ; $<2\%$ ^{225}Ra and a radio isotopic purity of 100% ^{225}Ac .

6 PARTNERS IRRADIATION CAPACITY (CURRENT AND FORESEEN)

Partners associated with this task are NNL, NRG, ILL, NCBJ and JRC-Karlsruhe (in consultation).

6.1 ILL

ILL operates a high-flux reactor with different irradiation positions reaching neutron fluxes up to $1.5 \cdot 10^{15} \text{ cm}^{-2}\text{s}^{-1}$. Thanks to the heavy water moderator the neutron flux at the irradiation positions is relatively well thermalized, i.e. thermal neutrons dominate over fast or epithermal neutrons. Consequently these irradiation positions are best suited for (n, γ) or (n,f) reactions but less for (n,p), (n, α) or (n,2n) reactions that would require fast neutrons.

Specifically an irradiation of ^{226}Ra would lead via (n, γ) β^- first to ^{227}Ac (that may be used as generator of ^{227}Th and ^{223}Ra) then via (n, γ) β^- (n, γ) β^- to ^{228}Th (that may be used as a generator of ^{224}Ra and ^{212}Pb respectively) and ultimately via (n, γ) β^- (n, γ) β^- (n, γ) to ^{229}Th (that after very long decay of disturbing ^{228}Th may be used as generator of ^{225}Ac).

6.2 NRG

At the Nuclear Research and Consultancy Group (NRG) in Petten, the Netherlands, a High Flux Reactor (HFR) is operated with a capacity of 45 MW. Operation is 24 hours per day continuously during about 27 days in one month. In total, the HFR's availability is about 265 full power days per year.

Types of products produced are:

- Fission products created by the irradiation of uranium targets (^{99}Mo and ^{133}Xe). The use of uranium requires active cooling to remove the high fission power density induced during irradiation.
- Short-lived isotopes (e.g. ^{177}Lu , $T_{1/2} = 6.7$ days). Since the half-life of these short-lived isotopes is much shorter than the cycle length of the HFR (1 month), these isotopes need to be unloaded when the reactor is in operation. This requirement results in a complicated facility design that allows for both loading and unloading of targets during operation.
- Long lived isotopes (e.g. ^{192}Ir , $T_{1/2} = 74$ days and ^{228}Th , $T_{1/2} = 1.9$ year). These isotopes are unloaded during a reactor stop.

All three of these groups are irradiated in a different type of irradiation facility.

There are several irradiation facilities available within the HFR. The typical target composition, geometry and encapsulation depend on the facility and purpose of irradiation. A typical target for material research is for instance steel or graphite and looks like samples that can be used for mechanical testing (e.g. tensile strength testing).

Simultaneously a new reactor (called PALLAS) is being built which is dedicated, mainly, for the production of medical isotopes. The reactor is expected to start up in 2030 and will temporarily run simultaneously with the HFR after which the HFR will be decommissioned.

6.3 Material Handling

6.3.1 ILL

Liquids cannot be used for irradiation. While noble gas targets are occasionally used, most targets are solid. These solids must remain solid also at the calculated elevated temperatures

they may reach during irradiation plus a safety margin. The actual shape can be disks, foils, wires, powder, “deposits” on various types of backings, etc.

Targets for nuclear physics applications at ILL’s fission fragment separator LOHENGRIN are “thin”, i.e. typically $<0.5 \text{ mg/cm}^2$ actinide layer, covering an area up to $7 \times 1 \text{ cm}^2$. This is illustrated in Figure 16. These targets are deposited onto a thick Ti backing and usually covered with a very thin $0.25 \text{ }\mu\text{m}$ Ni foil to limit self-sputtering. In the in-pile position the targets are exposed to a neutron flux of about $5 \cdot 10^{14} \text{ cm}^{-2}\text{s}^{-1}$. The fission fragments produced in thermal neutron-induced fission leave the target by the recoil energy obtained in fission, traverse the thin Ni foil and are separated by mass and kinetic energy in the LOHENGRIN recoil separator.



Figure 16. Example of a LOHENGRIN fission target already mounted on the Ti target holder and covered with a thin Ni foil.

Targets for production applications in the V4 beam tube need to be enclosed into multiple layers before irradiation. Usually the first layer is a sealed quartz ampoule. Filling and sealing of the quartz ampoule is usually performed outside ILL by the same collaborating lab to which the activated targets will be returned after irradiation at ILL.

At ILL one or several quartz ampoules are enclosed into an irradiation capsule with 20 mm inner diameter, 1 mm wall thickness and about 69 mm height after closing. After loading the ampoules into the capsules, the latter are closed by “cold-welding”, i.e. pressing a lid onto the capsule body. The cold-welding is performed under helium atmosphere after having pumped residual air out. Thus, activation of air is avoided and the helium atmosphere guarantees best thermal dissipation during irradiation. An example of a small foil target enclosed in a quartz ampoule before enclosure in an aluminium capsule is shown in Figure 17.



Figure 17. Example of a small metal foil target enclosed in a quartz ampoule to be enclosed into an aluminium capsule for irradiation at ILL.

The main function of the quartz ampoule is to keep the material to be irradiated “clean” during encapsulation, irradiation and decanning at ILL until it returns in irradiated form to the external lab. Formally, a quartz ampoule does not count as “strong” barrier, because it could, in principle, break. Therefore, its use is not mandatory if external contamination of the sample is acceptable and if the sample has a shape that can be handled directly with the manipulators of the hot cell, e.g. disks or wires can be placed directly into the capsule.

Since the closing of the Al capsules is performed in an environment that is not foreseen to handle open alpha activity, alpha active targets to be irradiated in V4 should arrive at ILL already enclosed into a welded metal capsule which is enclosed in turn into the Al capsule. Favourable metals for these internal capsules are *e.g.* Ti or V since these experience little durable activation in a high thermal neutron flux and can be shipped together with the contained irradiated sample to the collaborating lab that will perform the post-irradiation treatment of the target.

6.3.2 NRG

There are several irradiation facilities available within the HFR. The typical target composition, geometry and encapsulation depend on the facility and purpose of irradiation. A typical target for material research is for instance steel or graphite and looks like samples that can be used for mechanical testing (e.g. tensile strength testing). A typical target for medical isotopes irradiations at the HFR consists of the target material inside a closed quartz ampoule, which is placed inside an aluminium can that is welded shut in a helium atmosphere to provide an inert and leak-tight containment for the ampoule and in turn for the target material.

For the irradiation of ^{226}Ra material it was decided to perform the first irradiations with small amounts of ^{226}Ra in an open quartz ampoule in a sealed aluminium tube after which this was

placed in a double walled aluminium capsule. This configuration was chosen due to the lack of experience with handling ^{226}Ra and the fabrication of ^{226}Ra targets. For future experiments, a sealed quartz ampule will be used inside a double walled aluminium can.

To minimize pressure build-up during irradiation in the first target material containment, liquids or significant amounts of materials that cause gas release (e.g. due to dissociation) are to be avoided. In the case of ^{226}Ra , a very low amount of resource material is needed, which makes loading of the material in solid form into the ampule impractical. Therefore, the source material is dissolved and pipetted into a quartz ampule. The solvent is subsequently evaporated prior to closing of the first containment, leaving the target material deposited as a solid on the bottom of the ampule. The facilities that the HFR uses in-core are strictly confidential. Information that can be shared is that a coolant (water) is run directly around the standard cylindrical aluminium can noted in above and conservative cooling margins are used to ensure safe operation of the HFR.

Standard aluminium cans are always used for irradiation. Therefore, limited amounts of target material can be contained depending on the maximum allowable pressure build-up in the different containment layers. Initially, the target material was contained in an open quartz ampule covered with quartz wool to prevent particles from moving out of the quartz ampule. The ampule was then placed in an aluminium tube that is sealed via cold welding with a hydraulic press. This is in turn placed in a double walled aluminium can of standard measurements which is sealed via Tungsten Inert Gas welding (TIG welding) welding.

6.4 Quantities and Qualities of materials

6.4.1 ILL

There is no minimum mass. For test purposes targets with very small quantities (even ng) are best prepared in the form of “deposits” by deposition of a drop of a reference solution into a quartz ampoule and subsequent drying.

The maximum sample mass that can be irradiated is determined by different factors:

a) Available space

De facto the minimum dimensions are probably given by the smallest size of quartz ampoule that can be reasonably prepared. Even if not required for the purpose of “cleanliness” very tiny foil or wire samples should be enclosed into a quartz ampoule for easier handling with manipulators or tweezers in the hot cell during the decanning process.

Up to 4 ampoules with up to 8 mm diameter and up to 50 mm height can be placed into a capsule. Alternatively up to 3 ampoules with up to 9 mm diameter and 50 mm height or 1 ampoule with <20 mm diameter and ≤ 50 mm height.

For alpha emitter targets that arrive at ILL enclosed in a leak-tight welded metal capsule the latter has to fit into these dimensions, i.e. <20 mm diameter and ≤ 50 mm height.

b) Nuclear heating and thermal conductivity of the sample that leads to a calculated maximum sample temperature well below the melting point.

c) Calculated activities and dose rates after irradiation.

In particular the constraints b) and c) will lead to hugely varying sample mass depending on the sample element, isotope and chemical compound. While a pile of metallic molybdenum disks of several tens of grams per irradiation capsule would easily satisfy the requirements, much lower mass limits would be derived for samples with high capture cross-section leading to radionuclides (e.g. ^{176}Lu , Ir, etc.) or for fissile samples that would lead to higher heat deposition and stronger constraints from b).

6.4.2 NRG

The minimum mass of the target material is not defined. Theoretically, there is no minimum mass of the target, however the cost of irradiation has to be justified by the outcome of irradiation.

The maximum quantity of target material depends on:

Chemical composition of the target

The permissible amounts of impurities are mainly determined by a) additional dose rate from activation products and b) additional pressure build-up from decomposition during irradiation, c) processing steps after irradiation.

Strength of the containment

The containment consists of two or three layers depending on whether a closed or an open quartz ampoule is used. A complication in assessing the strength of the quartz ampoule is that the mechanical strength of the quartz might deteriorate during irradiation due to radiation induced embrittlement of the quartz. It seems that several parameters influence the embrittlement, *e.g.* quality of the quartz, neutron dose, neutron spectrum, irradiation temperature, duration. The issue with ^{226}Ra irradiations is that the irradiation time must be rather long to obtain sufficient amount of ^{228}Th , thereby increasing the risk of quartz fracture. The impact of neutron irradiation on the mechanical properties of the aluminium is much less significant.

Dose rate of the irradiated material

The dose rate of irradiated ^{226}Ra is mainly determined by the ^{208}Tl daughter of ^{228}Th . Computed dose rate values will be described in deliverables 1.2 and 1.3.

License and safety case for the processing facility

Deliverable 1.2 will discuss NRG's license for processing ^{226}Ra containing materials.

6.5 Radioactivity limits etc

6.5.1 ILL

For nuclear physics experiments with the LOHENGRIN spectrometer only fissile or fertile targets are of interest. So far targets of ^{229}Th , ^{233}U , ^{235}U , ^{237}Np , ^{239}Pu , ^{241}Pu , ^{241}Am , ^{245}Cm , ^{249}Cf and ^{251}Cf have been employed. In principle others could be used too, pending availability of material with suitable enrichment and purity.

For irradiations in V4 so far alpha-emitting targets containing ^{235}U , ^{237}Np , ^{241}Am , ^{245}Cm , ^{248}Cm , ^{250}Cf and ^{254}Es have been employed.

A formal limit of 3.7 GBq per target applies, but in most cases much tighter constraints will result from the limitations b) and c) under section above 6.4.1, or the contact dose rate during encapsulation and shuttle welding before irradiation. At present these tasks are performed manually which limits the allowable surface dose rate. An automated welding apparatus (cf. Task 1.5) would allow to reduce radiation exposure of the operators during these steps and consequently enable handling higher activities.

6.5.2 NRG

Depending on the chemical composition and purity, limits are set for the amount that is allowed in irradiation targets. For the irradiation of ^{226}Ra targets the starting point is:

Standard aluminium cans for irradiation are limited to 4 bar(abs), so with an atmospheric filling pressure of 1 bar(abs), the pressure increase must be limited to 3 bar (under hot conditions) above the original pressure. This maximum pressure is determined by the safety requirements/limits that are caused by the mechanical stability/strength of the aluminium capsules.

To determine that the target is safe to irradiate, several types of analysis are performed including gamma spectrometry, activation calculations and thermomechanical analysis and elemental analysis or inductively-coupled-plasma mass spectrometry (ICP-MS). Activation calculations are used to compute the type of nuclides formed during irradiation. Thermomechanical analysis (TMA) determines how target (materials) behave during irradiation and if this poses a risk to nuclear safety.

In other words, TMA determines if the integrity of the target materials is affected by irradiation, for example, due to pressure build-up or melting.

Several target configurations have been analysed. So far, irradiation with 0.12 mg and 0.25 mg of ^{226}Ra have been performed successfully. Safety analysis has been done for the future irradiation of 0.6 mg of ^{226}Ra and 0.6 mg targets have been prepared. For the 0.12 and 0.25 mg targets, the chemical composition was well known and quite pure. However, for the 0.6 mg targets, the material was significantly less pure than the previous batch of ^{226}Ra . This resulted in the need for very conservative assumptions when performing activation calculations and thermomechanical analysis. The results for 0.6 mg are reported in the Table 7.

Table 7. NRG's calculations for a 0.6 mg Ra226 target

Element	Atomic weight [g/mol]	Absolut mass in target [mg]	Number of atoms [mol]	Number of gas molecules [mol]
N	14	0.40	2.89E-05	1.44E-05
O	16	1.39	8.66E-05	4.33E-05
total				5.77E-05

As shown in Table 7, the maximum amount of nitrogen and oxygen gas that is caused by the complete dissociation of this target material is 5.77E-05 mol.

For the irradiation of 0.6 mg of ^{226}Ra maximum, thermomechanical analysis has calculated the maximum pressures during regular operation and in an accident scenario. One accident scenario assumes that the first containment with target material has been breached and leaks into the containment of the double walled aluminium can. The central temperatures and pressures in the containments have been presented in Table 8.

Table 8. Results of NRG's thermomechanical simulation. All pressures are absolute.

case	T _{central} [°C]	Closed kwarts ampule [bar]	1 st wall Aluminium capsule [bar]	2 nd wall Aluminium capsule [bar]
regular	565.9	2.4	1.6	1.4
accident scenario	416.9	2.4	2.4	1.4

As outlined in Table 8, in the accident scenario, there is no pressure difference between the quartz ampule and the first wall of the aluminium capsule as it is the closed kwarts ampule that has been breached. In the accident scenario the temperature decreases due to helium ingress in a space that was originally filled with air. The resulting pressures and pressure differences between the containments, and between the 2nd wall of the aluminium capsule and the reactor basin, do not surpass safety limits as the maximum allowable pressure for the 1st wall of the aluminium capsule is 2.84 bar.

6.5.3 Logistics

6.5.3.1 ILL

Compatibility with ILL's safety requirements will be checked by ILL before agreement to ship radioactive targets to ILL is given. In particular, a certificate of analysis of the target material and its enclosure (quartz or/and metal capsule) and a certificate of leak tightness of the metal encapsulation of alpha emitters is required.

Targets for nuclear physics experiments should arrive already deposited onto the Ti backing. In a glove box at ILL they will then be fixed by spot welding onto a Ti target holder and covered with a Ni foil.

Targets for irradiation in V4 should arrive already enclosed into quartz ampoules. Alpha-emitters should be enclosed into a welded and leak-tested metal capsule. At present the encapsulation and hot-welding into irradiation shuttles is performed manually. An upscaling of contained activity leading to significant surface dose rates would require an automatized welding apparatus, covered elsewhere in the SECURE programme, in Task 1.5. Once shipped and unpacked, alpha emitting samples will be stored in ILL's "Alpha lab" between arrival at ILL and irradiation.

All irradiated targets are returned to the previously agreed lab that will perform the post-irradiation processing. Before irradiation takes place, the expected post-irradiation activities will be calculated by ILL and shared with the collaborating lab. Only when this lab agrees to receive the irradiated target will the irradiation be performed.

After irradiation, the shuttles are stored under water to let short-lived activities such as ^{28}Al , ^{27}Mg , ^{56}Mn , etc. that are generated in the aluminium capsule and irradiation shuttle decay before further processing. Then the shuttle is moved into ILL's general purpose hot cell for the "decanning" operations where the irradiation shuttle is cut, the irradiation capsules are removed and cut to remove either the quartz ampoules or metal capsule containing alpha emitters respectively. These are then placed into a certified transport container (Type A or Type B) for shipment to external collaborating labs.

Transport packages have to be provided by the collaborating labs. The loading is performed in ILL's general purpose hot cell. For this purpose, the inner shieldings of the transport packages have to be craned into the hot cell, loaded and closed with manipulators, craned out and decontaminated before being placed into the transport package. Different shielding designs are more or less suited for remote-handled loading and closing with manipulators. Suitable containers are e.g. Posisafe KL-30 (Lemer Pax) or CF18T (Comecer) for Type A packages or Croft Safekeg for Type B packages.

6.5.3.2 NRG

The pre-irradiation storage consists of two stages:

- The incoming ^{226}Ra from the supplier of the ^{226}Ra . This material can be stored in its transport package in a dedicated vault for radioactive material. Storage conditions should be such that the dose rate outside the vault should be within radiological limits.
- The ^{226}Ra target that is ready for irradiation can be stored in the above-mentioned vault under the condition that it is suitably packed and the dose rate outside the vault stays under the radiological limits.

Facilities, glovebox equipment and available experimental equipment for target preparation at NRG are outlined and described in Table 9, Table 10, Table 11 in the Appendix.

Logistics at NRG

A license is always needed for storage, handling and specific activities if an organization wants to perform with ^{226}Ra in the quantities as have been handled in the above example. Safety cases are at the core of these licenses and should at the very least discuss the risks and hazards that the use of ^{226}Ra pose upon operators, the public and the environment.

Outlined below are the steps in producing at target prior to irradiation.

1. Receiving the resource material:

Transport of unirradiated ^{226}Ra to Petten has taken place in Type A containers. Thick PE sheets are used to seal the ^{226}Ra containing vial. Shielding of 3.2 cm of lead results in enough reduction in gamma radiation to be in accordance with Type A package requirements. The as-received container is transported on site according to the same standards as those for public transport.

2. Opening the resource material:

The resource material was contained in an RVS container with a hexagonal shaped indent for opening means. A dummy was fabricated and used to develop an opening tool. Figure 18 shows a picture of the dummy container.



Figure 18. NRG dummy container for transport

Figure 19 shows the cross section of the opening tool. RVS was used for the outer layer of the tool, but most of the inner material of the tool is made from the shielding material Densimet.

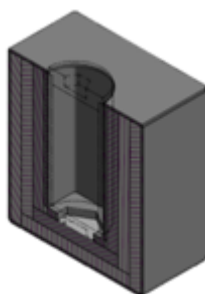


Figure 19. Cross section of the opening tool at NRG

3. Dismantling of the resource material:

After opening the can with a long tong, large tweezers are used to pick up the individual ^{226}Ra containing tubes and put them in a beaker. The 20 mL beaker is located in shielding as shown in Figure 20.

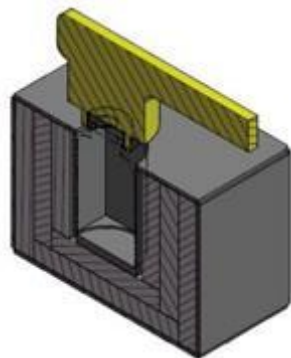


Figure 20. 20 ml beaker shielding at NRG

4. Conversion of chemical structure and purification:

After retrieval of the ^{226}Ra containing material from the individual sample holders, a series of chemical conversions and column chromatography steps were performed to arrive at $\text{Ra}(\text{NO}_3)_2$ target material of acceptable purity.

5. Posting out an aliquot for gamma spectrometry measurement:

An aliquot of the stock solution was taken and measured by gamma-spectroscopy to determine the yield of ^{226}Ra . The 50 μL aliquot was transported in a container with similar specifications to a type A container.

6. Filling the open quartz ampule:

After purification, a pipette is used to transfer an aliquot of 0.6 mg ^{226}Ra into a quartz ampule for irradiation.

7. Evaporating the solvent in the ampule:

For evaporating the target solution inside the quartz ampules, a shielding block is placed directly on the heating plate. A nitrogen flow aids the evaporation of the ^{226}Ra nitrate solution.

8. Placing the ampule in aluminium tube:

The open ampule is stopped with quartz wool and placed in the aluminium tube.

9. Cold welding of aluminium tube:

Cold welding is performed with a hydraulic press. No heat is used to close the aluminium capsule. However, for future targets, closed ampules are desired with flame-welding techniques.

10. Posting out the aluminium tube with target materials:

A standard transport cannister was used.

11. Cleaning the aluminium tube in the decontamination box:

To prevent contamination to other laboratories or irradiation facilities, Containment 1 with the target material is brought to the smaller glovebox which is designed for the decontamination of targets that will be irradiated.

12. Leak tests of the aluminium tube (or quartz tube):

Place the sealed aluminium capsule on a hotplate and warm it up somewhat, to increase the internal pressure, while checking for Rn release with a Rn probe.

In the future, closed quartz ampules will be produced through flame welding. After cleaning the sealed quartz ampule, the seal is inspected with an electronic microscope.

13. Welding and leak testing of the double walled aluminium can:

For immobilizing the aluminium tube, aluminium grout and aluminium foil are used to fill up empty space in the double walled aluminium can. Then, in a dedicated, helium-filled glovebox, the double walled aluminium can is sealed using TIG welding. Both the aluminium tube and the double walled aluminium can are leak tested after their respective welding steps. After

successful leak testing of the aluminium tube is completed, the welding of the double walled aluminium can take place. The double walled aluminium can also undergoes leak testing.

Post irradiation, the targets need to cool in the reactor pool for about a week before they can be processed in the glovebox in the Actinide lab. The reason for this is that the ^{226}Ra irradiation capsule is made of aluminium in which ^{24}Na ($t_{1/2} = 15$ hours) is formed during irradiation. The dose rate caused by ^{24}Na (directly after irradiation) is very high compared to the dose rate of the ^{226}Ra , which makes that a week's time is needed for ^{24}Na decay. During this week the dose rate from the decay of ^{228}Th is negligible compared to the dose rate resulting from ^{24}Na decay.

A transport container with heavy lead shielding (e.g. 18 cm in case of the HFR) is used for post- irradiation transport to the Actinide lab. More irradiation products, other than the ^{226}Ra target, are transported in this container at the same time (for transport efficiency and ALARA requirements). The dose that can be ascribed to the transport of the irradiated ^{226}Ra is about 3 micro-Sievert and is marginal compared to the other irradiation products transported in the container.

7 GENERAL CONCLUSIONS

Global demand for ^{225}Ac is greater than the amount that is currently available. Currently there are several different routes to ^{225}Ac , either from legacy material extraction or from transmutation of a target via an irradiation device. Several different irradiation routes have been presented, in terms of assessing the form that the targets need to take and how these targets are made. Specifically, this deliverable has addressed the form of the target relative to the production route specified, namely by proton, deuteron, gamma or neutron irradiation.

^{225}Ac can be transmuted from ^{226}Ra by proton irradiation to directly form ^{225}Ac , theoretically proposed via deuteron irradiation to produce ^{225}Ac , by gamma irradiation to produce ^{225}Ra , which decays with a 14.9 half-life to ^{225}Ac and by neutron irradiation, both thermal and fast. In many cases, the by-products produced are chemically indistinguishable from ^{225}Ac , which can pose challenges in post-irradiation purification unless utilising mass separation. Shorter lived isotopes such as ^{224}Ac ($T_{1/2} = 2.78$ h) and ^{226}Ac ($T_{1/2} = 29.37$ h) can be reduced by tailoring the post-irradiation cooling time, left to decay, but longer-lived isotopes such as ^{227}Ac ($T_{1/2} = 21.77$ y) should be minimised where possible. If ^{227}Ac can be separated from the desired product (such as in the case of production of ^{228}Th), there is a potential to use the ^{227}Ac for production of other desirable alpha-emitting isotopes, such as ^{223}Ra .

The target requirements that have been considered for routes to ^{225}Ac production are: legacy material via decay, proton irradiation, deuteron irradiation, gamma irradiation and by neutron irradiation (thermal and fast). Targets for ^{223}Ra production consider routes from legacy material via decay and potentially by utilising by-products of other irradiations. Targets for routes for ^{212}Pb production considers legacy material via decay and by neutron irradiation of ^{226}Ra .

The predominant irradiation target for these materials is ^{226}Ra regardless of irradiation type, either through single or multiple events, transmuting to ^{225}Ac directly or creating isotopes higher up in the decay chain and time given to decay. Potential legacy sources of ^{226}Ra , and their expected impurities, have been presented, but will be more fully extrapolated within other tasks.

Purity of the initial radium target material needs to be understood, and be able to be assessed to inform a decision whether the ^{226}Ra is purified before irradiation, and how likely the impurities are to cause an adverse effect, and whether the impurities, and potential transmuted impurities, are able to be more easily separated in post-processing steps. Extensive pre-purification of radium is not covered in this deliverable, except where captured in the target manufacturing steps. As a very reactive material, ^{226}Ra is not envisaged to be utilised in its metal form, and selection of the chemical form in which it is irradiated needs to be considered, in the ease of formation of the target, in terms of potential off-gas production, to be able to be utilised in the irradiation device, and in the post-processing requirements. An assessment should be made on an individual facility basis over the levels of tolerable impurities, type, and expected consequence.

Quantities, where given, are presented of ^{226}Ra sources, and different potential chemical forms of radium have been discussed, with their challenges and benefits. A brief introduction to some of the challenges of working with ^{226}Ra have been explored, but this is closely tied into infrastructural requirements which will be more fully covered in D1.2.

Information has been captured around the irradiation facilities available at NRG and at ILL, and some of the physical and logistical considerations described should a target be envisaged to be irradiated at these facilities.

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9 APPENDIX

Table 9. Facilities at NRG

#	Equipment name:	Elucidation:
	Actinide Laboratory	Laboratory developed to handle -alpha emitters, originally uranium, plutonium and americium. Currently, ^{226}Ra (irradiated or unirradiated) can also be processed here. The facility is licenced to handle unirradiated and irradiated ^{226}Ra targets.
	Type B laboratory	Laboratory of NRG in which radioactive materials can be used up to 2000 Re per activity. The "Re" stands for "Radiological Equivalent" and means that when one Re is ingested or inhaled the dose consequence is 1 Sv. Samples are analysed here using gamma spectrometry.
	Pre-irradiation transport cannisters	Cannisters that are for on-site transport of radioactive materials that are already well contained without the cannister. Can be docked, loaded and unloaded onto almost all facilities on site.
	Docking system on the glovebox	This is used to retrieve or deliver ^{226}Ra material into the glovebox. Up to 1.2 mg of irradiated ^{226}Ra can be handled in the glovebox, this equals the two 0.6 mg targets fabricated.
	Nitrogen gas flow	Dry nitrogen gas is used as for the glovebox atmosphere and for the chemical setup (e.g. during evaporation or liquid transfer steps).
	Post-irradiation transport container	A container with 18 cm lead shielding is used for on-site transport of irradiated materials. On site transport does not need licensing as the roads are not public. However, safety measures are taken as if it were a public road.
	Glovebox	Glovebox at a negative pressure of 260-300 Pa in the Actinide Laboratory to safely handle the unirradiated ^{226}Ra .

Table 10. Glovebox Equipment at NRG

Charcoal filter of chemical set-up	Charcoal filter through which the nitrogen flow from the chemical process' tubing is filtered before being discharged to the off-gas. In this way, as much as possible, it is avoided that radioactive particles enter the glovebox. Thereby trying to keep the glovebox as clean as possible.
Charcoal filters of the glovebox #1 and #2	Charcoal filter of the glovebox from where the outgoing nitrogen flow moves to the off-gas. There are two identical filters in parallel with a switch to select which filter is currently active. This allows for trapping of released Rn gas until decayed to minimise Rn emissions into the off-gas. Due to the 3.6 days half-life of ²²² Rn, the switching of the filter cannot be done very frequently, since some decay of the ²²² Rn is needed before switching is meaningful.
Radon probe	A radon probe is used to measure radon release to the off-gas. The data on the concentration of radon isotopes can be collected online or offline.
HEPA filter	Particle filter stopping dust particles and aerosols after the charcoal filters, but before the radon probe.
Flow control unit	Used for regulating the nitrogen flow to the chemical set up.
Containment 2: Outer aluminum capsule	Outer aluminium capsule.
Containment 1: Inner aluminum capsule	Inner aluminium capsule
Reducing valve	Valve that limits the maximum amount of nitrogen flow towards the glovebox.
Polaris camera	<p>Gamma spectrometry camera for characterizing samples in the glovebox. At the start of activities, the gamma camera should read <10 MBq for the coal filters.</p> <p><i>If the activity of the coal filter is ≥ 10 MBq and an unforeseen large release of Rn gas takes place, this would require for the coal filters to be switched. Hereby, the 10 MBq which is equal to ~ 0.1 Re ($1 \cdot 10^6$ Bq * $1.1 \cdot 10^{-8}$ Sv/Bq), will be set free in the off-gas and thereby the environment.</i></p> <p>At the end of a procedure or working day, check if the radon peak value in the glovebox has exceeded 2 MBq/m³. If this is the case, it should be discussed which approach should be taken for the coal filters. Hereby, the activity of the coal filters, as determined in step 8, and the cumulative radon release, as determined in step 6, are taken into consideration. It might be necessary, especially if an open handling has taken place, to switch the coal filters. Note down in the logbook if the coal filters are changed.</p> <p><i>Preferably, a working day after radon release (assuming a peak release), coal filters are switched. The exact timing, and thus the preferred working day, of switching from one filter to the other filter is only relevant when a significant amount of radon is released into the glovebox. A significant amount is defined as more than 2 MBq/m³ inside the glove box as the peak value during processing. Release of this amount leads to a release of 0.02 Re (2 MBq/m³ * 0.88 m³ (volume glovebox) * $1.1 \cdot 10^{-8}$ Sv/Bq).</i></p>

Table 11. Experimental equipment for target preparation at NRG

Non-radioactive barium	For cold-testing of the chemical set-up.
Barium-133	Low radioactive barium, diluted in non-radioactive barium for semi-cold testing of the chemical set-up.
Separation column	Column used for separating different elements (including Ra and Pb).
Quartz ampule	Open quartz ampule as for depositing the radium target material.
Quartz wool	Material used in the top of the open quartz ampule to minimize radium dust particles flowing out of the ampule during transport and irradiation.
Peristaltic pumps	Pumps placed inside the glovebox are used for transferring liquids from stock solutions into the desired processing steps or mixtures.
Opening tool	An opening tool was designed for the source material container with added Densimet shielding integrated in the tooling material.
Tubes	Silicone en PTFE (polytetrafluoroethylene) tubing for transferring liquids between processing steps as part of the radio-chemical set-up.
Check valves	Check valves to prevent unwanted backflow of liquid or gasses in the process.
Combined heating-stirring plate	A combined heating-stirring plate is used for chemical processing steps.
Gas trap	Series of gas washing bottles filled with sodium hydroxide solution in order to remove condensable and water soluble species from entering the coal filters.
Pipette	The final ^{226}Ra solution is manually pipetted into the target container to prevent losses and minimize radioactive contamination of tubing.
Septa + needles	For transferring liquids.
Aluminium container + hydraulic press	First cold-welded containment.
Waste container	Container to collect liquid "waste" in the glovebox from the chemical processes taking place in the glovebox.