

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AdvanCell Pty Ltd.
Petitioner

v.

Sciencons AS
Patent Owner

Post Grant Review No.: PGR2025-00040

**PETITION FOR POST GRANT REVIEW OF
U.S. PATENT NO. 12,249,437**

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INDEX OF EXHIBITS

Exhibit No.	Description
1001	U.S. Patent No. 12,249,437.
1002	Declaration of Saed Mirzadeh.
1003	Hassfjell, Sindre P. and Hoff, Per, “A Generator for Production of ²¹² Pb and ²¹² Bi”, Appl. Radiat. Inst., vol. 45, no. 10, pp 1021-25 (1994) (“ Hassfjell-Hoff ”).
1004	WorldCat Index for Hassfjell-Hoff .
1005	International Publication Number WO 01/60417.
1006	File History of U.S. Patent No. 12,249,437.
1007	U.S. Patent No. 5,038,046 (“ Norman ”).
1008	International Atomic Energy Agency, “Radiotracer Generators for Industrial Applications”, IAEA Radiation Technology Series No. 5, IAEA, Vienna (2013) (“ IAEA ”).
1009	Westrøm, Sara; Generalov, Roman; Bønsdorff, Sara B.; and Larsen, Roy H., “Preparation of ²¹² Pb-labeled monoclonal antibody using a novel ²²⁴ Ra-based generator solution”, Nuclear Medicine and Biology, vol. 51, pp 1-9 (August 2017) (“ Westrøm ”).
1010	WorldCat Index for Westrøm .
1011	Hassfjell, Sindre, “A ²¹² Pb generator based on a ²²⁸ Th source”, Appl. Radiat. Isot., vol. 55, no. 4, pp 433-439 (2001) (“ Hassfjell-2001 ”).
1012	U.S. Patent Application Publication No. 2006/0286130 (“ Bhagwatwar ”).
1013	U.S. Patent No. 2,130,523.
1014	WorldCat Index for IAEA .
1015	U.S. Patent No. 6,592,843.
1016	Xanjiao Xie, “Dissolution, Formation, and Transformation of the Lead Corrosion Product PbO ₂ : Rates and Mechanisms of Reactions that Control Lead Release in Drinking Water Distribution Systems”, All Theses and Dissertations (ETDs), 387 (January 2010), available at https://openscholarship.wustl.edu/etd/387 (“ Xie ”).
1017	U.S. Patent No. 9,281,089.
1018	U.S. Patent No. 6,932,111 (“ Ishigaki ”).
1019	Declaration of Per Hoff.
1020	WorldCat Index for Xie .

CHART OF CLAIMS	
[1pre]	A radioisotope generator comprising:
[1a]	a solid precursor isotope source configured to emanate one or more gaseous progeny isotopes,
[1b]	the solid precursor isotope source comprising a precursor isotope; and
[1c]	wherein the solid precursor isotope is configured to be fluidly coupled to a volume including a collector surface with a gas tight seal, and
[1d]	wherein the solid precursor isotope source and the collector surface are configured such that the one or more gaseous progeny isotopes deposit one or more solid progeny isotopes on the collector surface.
[2]	The radioisotope generator of claim 1, further comprising a flushing circuit configured to flush the collector surface.
[3]	The radioisotope generator of claim 1, further comprising a valve associated with the solid precursor isotope source.
[4]	The radioisotope generator of claim 1, further comprising a vacuum pump attached to the volume.
[5]	The radioisotope generator of claim 1, wherein the solid precursor isotope source comprises a porous material configured to retain the precursor isotope.
[6]	The radioisotope generator of claim 5, wherein the precursor isotope is absorbed, adsorbed, and/or encapsulated by the porous material.
[7]	The radioisotope generator of claim 1, wherein the precursor isotope comprises a thorium 228 isotope (^{228}Th) and/or a radium 224 isotope (^{224}Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (^{220}Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (^{212}Pb).
[8]	The radioisotope generator of claim 1, wherein the collector surface is an interior surface of a container, and wherein the volume is an internal volume of the container.
[9]	The radioisotope generator of claim 8, wherein the solid precursor isotope source is configured to be connected to an opening of the container.
[10]	The radioisotope generator of claim 8, further comprising the container.
[11]	The radioisotope generator of claim 10, wherein the container is configured to removably connect to the solid precursor isotope source.
[12a]	The radioisotope generator of claim 10, further comprising a chelator disposed on the interior surface,
[12b]	the chelator configured to chelate the one or more solid progeny isotopes.
[13]	The radioisotope generator of claim 12, wherein the chelator comprises TCMC.

CHART OF CLAIMS	
[14]	The radioisotope generator of claim 10, wherein the volume is configured to receive a solvent configured to dissolve the one or more solid progeny isotopes from the interior surface.
[15]	The radioisotope generator of claim 1, wherein the radioisotope generator is configured to be converted from a first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source, and a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source.
[16pre]	A method of generating a progeny radioisotope, the method comprising:
[16a]	allowing one or more gaseous progeny isotopes to emanate from a solid precursor isotope source,
[16b]	the solid precursor isotope source comprising a precursor isotope;
[16c]	fluidly coupling a volume including a collector surface to the solid precursor isotope source using a gas tight seal; and
[16d]	allowing one or more solid progeny isotopes of the one or more gaseous progeny isotopes to deposit on the collector surface.
[17]	The method of claim 16, further comprising flushing the collector surface.
[18]	The method of claim 16, wherein fluidly coupling the volume to the solid precursor isotope comprises opening a valve associated with the solid precursor isotope source.
[19]	The method of claim 16, further comprising drawing a vacuum in the volume.
[20]	The method of claim 16, wherein the solid precursor isotope source comprises a porous material configured to retain the precursor isotope.
[21]	The method of claim 20, wherein the precursor isotope is absorbed, adsorbed, and/or encapsulated by the porous material.
[22]	The method of claim 16, wherein the precursor isotope comprises a thorium 228 isotope (^{228}Th) and/or a radium 224 isotope (^{224}Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (^{220}Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (^{212}Pb).
[23]	The method of claim 16, wherein the collector surface is an interior surface of a container, and wherein the volume is an internal volume of the container.
[24]	The method of claim 23, further comprising connecting the solid precursor isotope source to an opening of the container.
[25]	The method of claim 23, further comprising removably connecting the solid precursor isotope to the container.
[26]	The method of claim 23, further comprising chelating the one or more solid progeny isotopes using a chelator disposed on the interior surface.

CHART OF CLAIMS
[27] The method of claim 26, wherein the chelator comprises TCMC.
[28] The method of claim 23, further comprising receiving a solvent in the volume, and dissolving the one or more solid progeny isotopes from the interior surface in the solvent.
[29] The method of claim 16, wherein fluidly coupling the volume to the solid precursor isotope source comprises converting a radioisotope generator from a first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source to a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source.
[30] The method of claim 16, further comprising forming a radiopharmaceutical using the one or more solid progeny isotopes.
[31] The method of claim 18, further comprising closing the valve to isolate the volume from the solid precursor isotope source.
[32] The method of claim 16, wherein the solid precursor isotope is bound to a non-radioactive material.
[33] The method of claim 32, wherein the non-radioactive material is a ceramic.
[34] The method of claim 23, forming at least a portion of a single chamber with the solid precursor isotope source and the container.
[35] The radioisotope generator of claim 3, wherein the valve is configured to isolate the solid precursor isotope from the volume in a closed position.
[36] The radioisotope generator of claim 1, wherein the solid precursor isotope is bound to a non-radioactive material.
[37] The radioisotope generator of claim 36, wherein the non-radioactive material is a ceramic.
[38] The radioisotope generator of claim 10, wherein the solid precursor isotope source and the container form at least a portion of a single chamber when fluidly coupled.

I. INTRODUCTION

AdvanCell Isotopes Pty Ltd. (“Petitioner”) hereby petitions for post-grant review of claims 1-38 (“Challenged Claims”) of U.S. Patent No. 12,249,437 (EX1001, “the 437 patent”).

Petitioner certifies that the 437 patent is available for post-grant review and that Petitioner is not barred or estopped from requesting a post-grant review (“PGR”) challenging the patent claims on the grounds identified in this Petition. *See* 37 C.F.R. §42.201.

Petitioner is filing this Petition within nine months of the 437 patent’s issue date (March 11, 2025), and this Petition is therefore timely. *See* 37 C.F.R. §42.202.

The 437 patent is eligible for PGR because its earliest priority date claimed is December 5, 2019. *See* AIA §3(n)(1).

II. STATEMENT OF PRECISE RELIEF REQUESTED

Petitioner requests cancelation of claims 1-38 of the 437 patent in view of the following grounds:

Ground	Claims	Stat. Basis	Prior Art
1	1, 3-4, 7-12, 14-19, 22-26, 28-29, 31-32, 34-36, 38	102	Hassfjell-Hoff
2	1, 3-4, 7-12, 14-19, 22-26, 28-29,	103	Hassfjell-Hoff

Ground	Claims	Stat. Basis	Prior Art
	31-32, 34-36, 38		
3	1, 3, 5-7, 15-16, 18, 20-22, 29-33, 35-37	102	Norman
4	1, 3, 5-7, 15-16, 18, 20-22, 29-33, 35-37	103	Norman
5	1, 3-12, 14-26, 28-38	103	Hassfjell-Hoff and Norman
6	2	103	Hassfjell-Hoff and IAEA
7	13, 27	103	Hassfjell-Hoff and Westrøm
8	8-12, 14, 17, 23-26, 28, 34, 38	103	Norman and Hassfjell-Hoff
9	13, 27	103	Norman, Hassfjell-Hoff, and Westrøm
10	13, 27	103	Hassfjell-Hoff, Norman, and Westrøm
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III. THE 437 PATENT

A. Overview of the 437 patent

The 437 patent describes a method and a system for producing highly purified ^{212}Pb , a radioactive isotope utilized in targeted alpha therapy for cancer treatment. EX1001, cls. 1, 16, 9:64-67. The process involves isolating and purifying ^{212}Pb from mixtures containing other isotopes through a specific decay chain that begins with ^{228}Th . EX1001, Fig. 1. The resulting ^{212}Pb is intended for

use in producing radiopharmaceuticals, enhancing the effectiveness of cancer therapies. EX1001, 17:18-21. The earliest claimed priority date for this patent is December 5, 2019 EX1001, cover. EX1002, ¶¶29-30.

B. Overview of the 437 patent's File History

The application that issued as the 437 patent underwent very limited prosecution at the U.S. Patent and Trademark Office. The examiner never issued any rejection during prosecution of this application, let alone one based on the prior art in this Petition. EX1006. EX1002, ¶¶31-32.

C. Person of Ordinary Skill in the Art

A person of ordinary skill in the art at the time of the alleged invention of the 437 patent (December 5, 2019) (“POSITA”) would have had a bachelor’s degree in chemistry, nuclear chemistry, radiochemistry, chemical engineering, physics, or materials science, or a comparable field of study, plus approximately two to three years of professional experience with radioisotope generators, radiopharmaceutical chemistry, nuclear medicine, or other relevant industry experience. Additional graduate education could substitute for professional experience, and significant experience in the field could substitute for formal education. EX1002, ¶33. EX1019, ¶27.

D. Claim Construction

The Challenged Claims are interpreted using the same claim construction standard that is used to construe the claim in a civil action in federal district court.

37 C.F.R. § 42.100(b). Petitioner does not contend that its proposed constructions are complete constructions of these limitations or the claims for any other purpose, including for issues that may be raised in a future litigation. Because the prior art asserted herein discloses the preferred embodiment within the indisputable scope of the claims, the Board need not construe the outer bounds of the claims as part of these proceedings. Any claim terms not listed below should be construed according to their plain and ordinary meaning to a POSITA at the time of the 437 patent.

EX1002, ¶34.

1. **“fluidly coupled”** (claims 1, 16, 18, 29, and 38)

The 437 patent specification does not recite the term “fluidly coupled.” The specification does disclose a system with parts capable of being connected or linked together using a gas. EX1001, Figs. 1-2, 5:17-24 (“an assembly comprising a first part and a second part, wherein the first part comprises a container and the second part comprises a ^{212}Pb precursor isotope source, wherein the first part and the second part are connected such that the ^{212}Pb precursor isotope source does not come into contact with an inner wall of the container, and such that a single chamber container assembly is provided.”). A POSITA therefore would have understood “fluidly coupled” in light of the specification to mean capable of being connected or linked together using a gas. EX1002, ¶35.

2. “wherein the solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface with a gas tight seal” (claim 1)

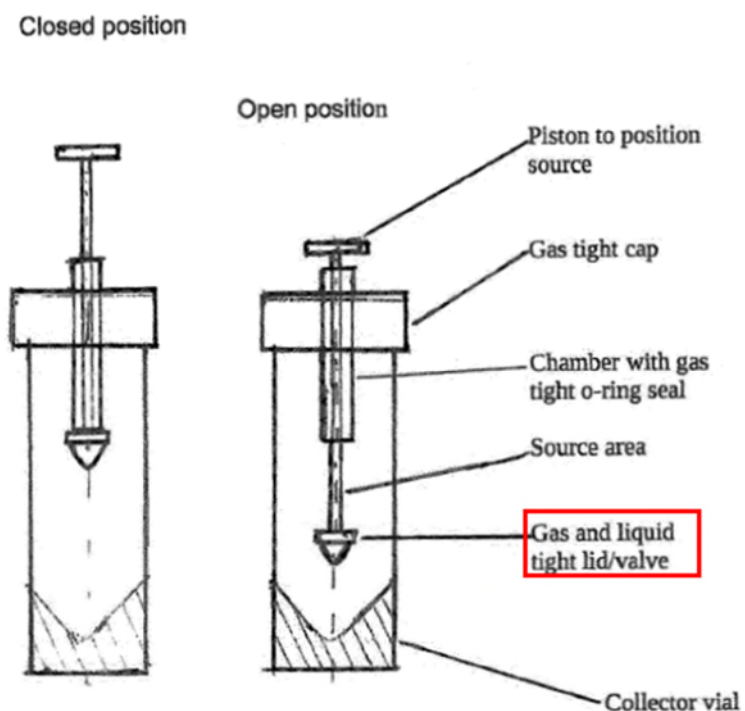
This limitation is ambiguous because it is not clear whether the phrase “with a gas tight seal” corresponds to “configured to,” “fluidly coupled,” or “volume.”

Thus, there are three possible constructions:

- The entire volume has a gas tight seal (with the precursor isotope source inside the volume),
- Just the collector surface, not the entire volume, has a gas tight seal (when the precursor isotope source is inside the collector), or
- The system is configured to selectively couple, using a gas tight seal, a volume with the solid precursor isotope source and a volume with a collector surface.

EX1002, ¶36.

Under the first possible construction, a POSITA would have understood the gas-tight seal of this limitation to include a gas-tight seal that selectively fluidly couples the precursor isotope source to a volume, as shown in Figure 4.



EX1001, Fig. 4, 14:21-25, 18:21-23. Alternatively, under the second possible construction, this limitation should be construed to require that the precursor isotope source is fluidly coupled to a fully enclosed volume that has a gas-tight seal, such as with Figures 3 and 5.



Fig. 3A



Fig. 3B

EX1001, Figs. 3A-B.



Fig. 5A

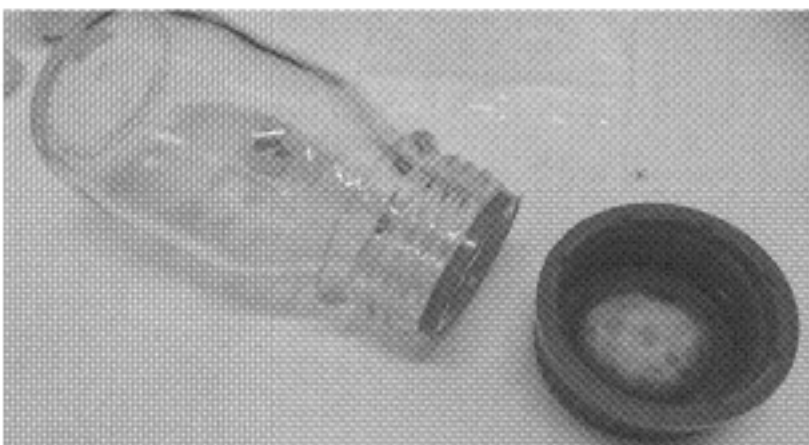


Fig. 5B

EX1001, Figs. 5A-B. Petitioner addresses these possible constructions, including the third construction, in the grounds below. EX1002, ¶¶37-39.

3. **“a valve associated with the solid precursor isotope source”**
(claim 3)

A POSITA would have understood “associated” to mean “to be used with.” Thus, a POSITA would have understood this term to include a valve that is used in combination with a solid precursor isotope source. EX1002, ¶40.

4. **“connected to an opening of the container”** (claim 9)

All disclosed embodiments of the 437 patent have a source connected to a cap which is then connected to a container’s opening. EX1001, Figs. 2-5, 8:48-53. In other words, the source need not be directly connected to an opening of a container. Thus, a POSITA would have understood that the term “connected” include both a direct or an indirect physical connection to the opening of the container. EX1002, ¶41.

5. **“removably connect”** (claim 11)

All disclosed embodiments of the 437 patent have a source connected to a removable cap which is then connected to a container’s opening. EX1001, Figs. 2-5, 8:48-53 Thus, a POSITA would have understood that the term “removably connect” includes both a direct or an indirect physical connection that is removable. EX1002, ¶42.

6. **“with”** (claim 34)

Claim 34 requires “forming...a single chamber **with** the solid precursor isotope source and the container.” The solid precursor isotope source does not

itself form the boundaries of a chamber in any embodiment of the 437 patent. *See* EX1001, Figs. 2A-2B, 8:48-53, Figs. 3A-3B, 14:25-36, Figs. 4A-4B, 14:37-43, Figs. 5A-5B, 14:44-50. Instead, all disclosed embodiments have a source connected to a cap which is then connected to a container's opening, such that the source is located inside the chamber. EX1001, Figs. 2-5, 8:48-53. To construe claim 34 consistent with the disclosed embodiments of the 437 patent, a POSITA would have understood the term "with" in claim 34 means "that includes." EX1002, ¶43.

IV. GROUND 1: CLAIMS 1, 3-4, 7-12, 14-19, 22-26, 28-29, 31-32, 34-36, AND 38 ARE ANTICIPATED BY HASSFJELL-HOFF

A. Hassfjell-Hoff

Hassfjell-Hoff is a journal article published in 1994 and entitled "A Generator for Production of ^{212}Pb and ^{212}Bi ." EX1003, 1-6. Hassfjell-Hoff was included in volume 45, number 10, of the "Applied Radiation and Isotopes" Journal (EX1003, 5 (Contents)), which was published in October 1994. EX1003, 1 (cover page); EX1004. Volume 45, number 10, of the "Applied Radiation and Isotopes" Journal was assigned ISSN 0969-8043 (EX1003, 5) and was received by the University of Wisconsin's Health Sciences Library on November 11, 1994. EX1003, 1 (cover page). As such, Hassfjell-Hoff was published and available to the public no later than November 11, 1994. EX1003, 1. EX1002, ¶44. EX1019, ¶¶29-31.

Hassfjell-Hoff was publicly accessible and indexed as a publication in public catalogs such as *e.g.*, the WorldCat index. EX1004. As further evidence of its public accessibility, Hassfjell-Hoff was cited in an International Patent Application naming inventor Roy Larsen (same inventor as the 437 patent) directed to analogous art that published on August 23, 2001, which proves both that (i) Hassfjell-Hoff was published to those of skill in the art at least as early as that date, and (ii) which itself serves as an index for Hassfjell-Hoff. EX1005, 10:17-18; *see also* EX1015, 7:67-8:1, 13:39-41. A POSITA would have understood that journals (*e.g.*, EX1003) and published patent applications (*e.g.*, EX1005) are reliable sources for information and would have been capable of accessing them well before the alleged filing date of the 437 patent. Accordingly, Hassfjell-Hoff qualifies as prior art under (post-AIA) 35 U.S.C. §102(a). EX1002, ¶45.

Hassfjell-Hoff discloses a radioisotope generator for the production of α -emitting radionuclides. EX1003, 6. Figures 2 and 3 show the disclosed generator:

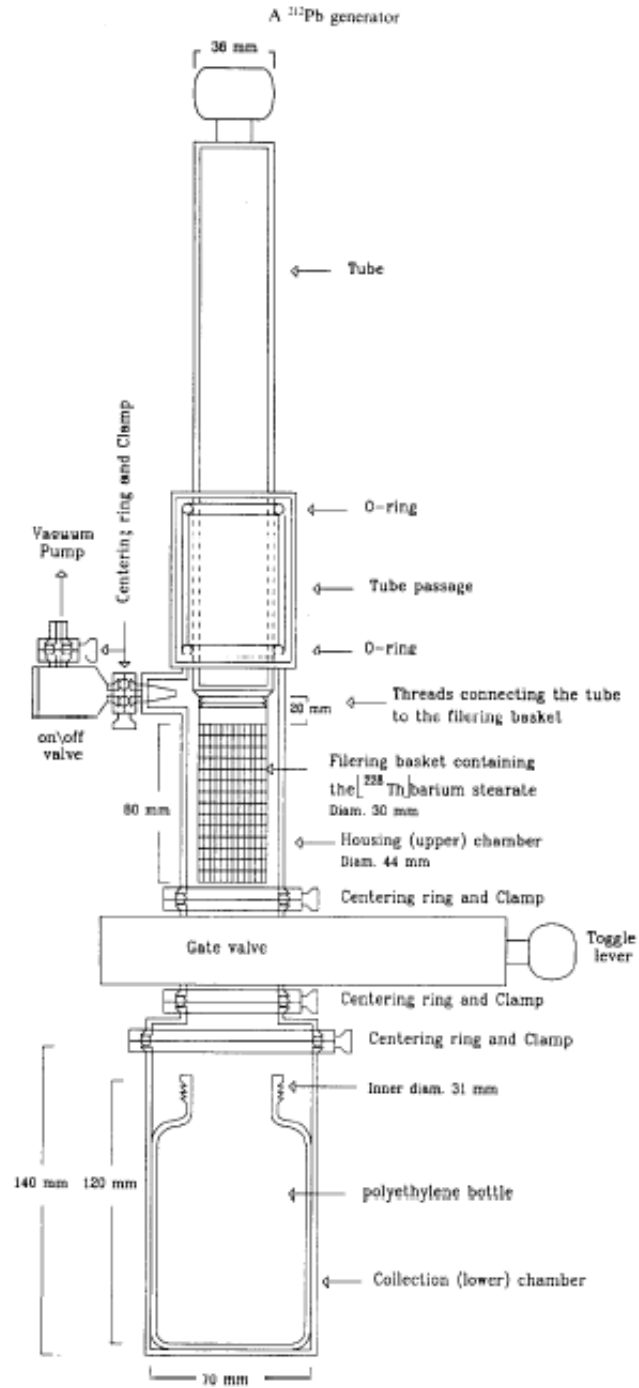


Fig. 2. The design of the generator showing functional details and operating mechanism.

EX 1003, Fig. 2.

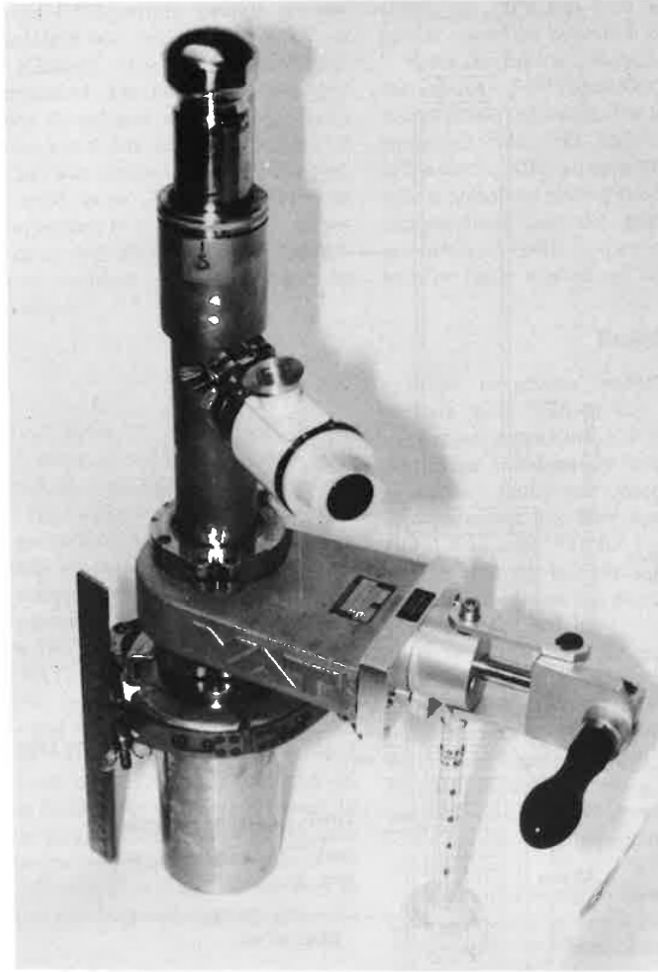


Fig. 3. A picture of the generator.

EX1003, Fig. 3. “The generator is based on the emanation of ^{220}Rn from $[\text{}^{228}\text{Th}]$ barium stearate.” EX1003, 6. The decay product of ^{220}Rn , which is ^{212}Pb , is deposited on the walls of a polyethylene bottle and can be washed off with distilled water. EX1003, 6. Hassfjell-Hoff discloses the construction of the generator shown in Figures 2 and 3:

All generator parts were made of stainless steel, and connected to standard high vacuum equipment to avoid leakage of radioactivity to the surroundings. The

generator was made with two compartments, a lower compartment which is a collection chamber and an upper compartment which is a housing chamber for the source when the collection chamber is removed. These two compartments are connected via a gate valve (VAT). The packets of [^{228}Th]barium stearate are placed in a filering basket¹ mounted by threads to the end of a long tube closed in both ends.... The tube can slide on two O-rings, thus facilitating the filering basket to move between the two chambers, through the gate valve.

EX1003, 7. “[A] polyethylene bottle is placed inside the collection chamber” to collect the emanated ^{212}Pb . EX1003, 7. Hassfjell-Hoff discloses how the generator was operated:

When the tube is lowered, the filering basket with the emanating [^{228}Th]barium stearate becomes positioned inside the bottle. The decay products from the emanated ^{220}Rn , ^{212}Pb and ^{212}Bi , deposit on the walls of the bottle. After an appropriate collection time, the tube is pulled up, placing the ^{228}Th source in the upper compartment,

¹ Throughout Hassfjell-Hoff, the document refers to a “filering basket.” Based on an online Norwegian-English dictionary, the meaning of the word “filering” is “a lace-like material.” See <https://glosbe.com/nb/en/Filering>. EX1002, ¶fn. 1.

EX1019, ¶fn. 1.

and the gate valve is closed. The polyethylene bottle is then removed and the radioactivity easily washed off with a suitable solution.

EX1003, 7. EX1002, ¶46. EX1019, ¶32.

The [^{228}Th]barium stearate packets are made using conventional means by taking [^{228}Th]barium stearate precipitated from a solution, filtering it onto filter membrane and washing it with methanol. EX1003, 6-7. The filter membrane with the precipitate is then folded and wrapped up into two additional filters to avoid any loss of [^{228}Th]barium stearate. EX1003, 7. The packets are then secured with plastic strips. EX1003, 7. EX1002, ¶47. EX1019, ¶33.

Hassfjell-Hoff is analogous art to the 437 patent. EX1001; EX1006. Moreover, as shown below, it was a material error for certain claims of the 437 patent to issue over Hassfjell-Hoff. EX1002, ¶¶48-49.

B. Claim 1

Hassfjell-Hoff discloses this claim arranged as claimed and in an enabling manner. EX1002, ¶¶50-58. EX1019, ¶¶29-38.

1. [1pre] “A radioisotope generator comprising:”

Hassfjell-Hoff discloses the preamble. Hassfjell-Hoff discloses a radioisotope generator used to generate progeny radioisotopes:

A generator has been developed for the production of the α -emitting radionuclide ^{212}Bi and its parent nuclide ^{212}Pb .

The generator is based on the emanation of ^{220}Rn from ^{228}Th barium stearate. The decay product of ^{220}Rn , ^{212}Pb deposits on the walls of a polyethylene bottle, and can be washed off with distilled water.

EX1003, Abstract.

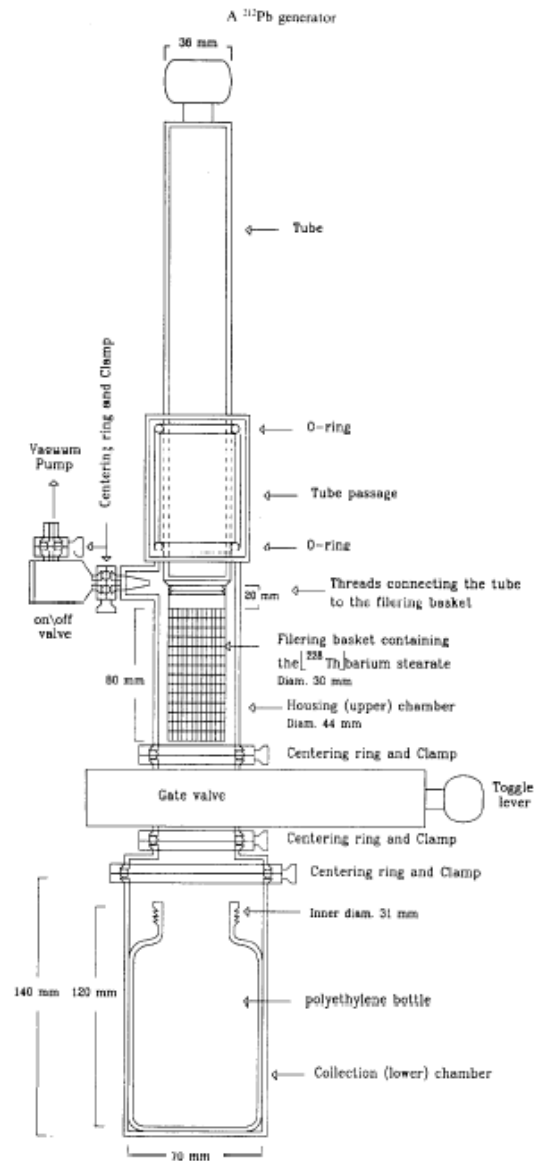


Fig. 2. The design of the generator showing functional details and operating mechanism.

EX1003, Fig. 2. EX1002, ¶51. EX1019, ¶¶29-38.

2. [1a] “a solid precursor isotope source configured to emanate one or more gaseous progeny isotopes”

Hassfjell-Hoff discloses this limitation. Hassfjell-Hoff discloses that the radioisotope generator includes a *solid precursor isotope source* (i.e., packet of [²²⁸Th]barium stearate). See EX1003, Abstract, 7. The *precursor isotope source* is prepared by a known method that results in the [²²⁸Th]barium stearate being precipitated from a solution onto a filter membrane. EX1003, 6-7. Hassfjell-Hoff’s “Gelman, U.S.” filter membrane with the [²²⁸Th]barium stearate precipitate is a *solid* that is formed into packets. EX1003, 7. A POSITA would have understood “Gelman, U.S.” to refer to a well-known supplier of filter membranes and that such membranes are solid made from 0.2 µm nylon 66 sterilizing grade. See EX1012, [0014], [0041], [0047]-[0049]. Nylon 66 is solid because it is a linear polyamide and melts at 190-195°C. EX1013, 6, right, 55-57. Thus, when the [²²⁸Th]barium stearate precipitate is formed into the membrane packet, it forms a solid. EX1002, ¶52. EX1019, ¶¶29-38.

Hassfjell-Hoff further discloses that the *solid precursor isotope source* (i.e., packet of [²²⁸Th]barium stearate) is configured to *emanate one or more gaseous progeny isotopes*. Hassfjell-Hoff discloses:

When the tube is lowered, the filtering basket with the emanating [²²⁸Th]barium stearate becomes positioned inside the bottle. The decay products from the emanated ²²⁰Rn, ²¹²Pb and ²¹²Bi, deposit on the walls of the bottle.

EX1003, 7. Figure 1 of Hassfjell-Hoff depicts the decay mode of ^{228}Th to the therapeutically desired ^{212}Pb , including intermediate and subsequent isotopes.

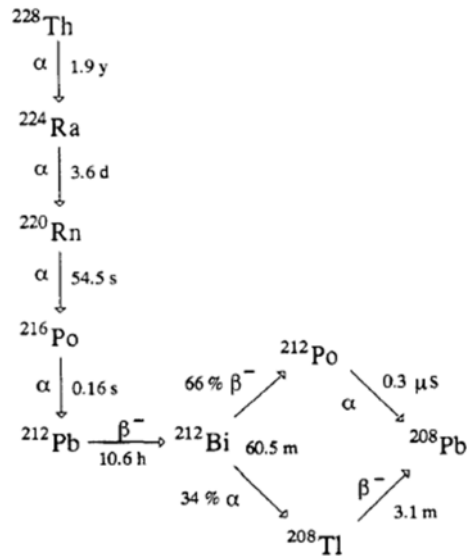


Fig. 1. The decay mode of ^{228}Th to stable ^{208}Pb .

EX1003, Fig. 1. One of those intermediate isotopes is “Rn gas,” which is a *gaseous progeny isotope* that behaves “based on the well-known Rn emanation.” EX1003, 6, Fig. 1. EX1002, ¶53. EX1019, ¶¶29-38.

3. [1b] “the solid precursor isotope source comprising a precursor isotope; and”

Hassfjell-Hoff discloses this limitation. Hassfjell-Hoff discloses a solid precursor isotope source (*i.e.*, packet of [^{228}Th]barium stearate). See §IV(B)(2) (limitation 1a). Hassfjell-Hoff discloses that the solid precursor isotope source comprises a precursor isotope (*i.e.*, ^{228}Th). EX1003, 7. EX1002, ¶54. EX1019, ¶¶29-38.

4. [1c] “wherein the solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface with a gas tight seal, and”

a. First Construction

Hassfjell-Hoff discloses this limitation according to the first construction provided above: that the gas-tight seal selectively fluidly couples the precursor isotope source to a volume. See §§III(D)(1), (2) (construction of “fluidly coupled” and limitation 1c first construction). EX1002, ¶55. EX1019, ¶¶29-38.

As shown in Figure 2, Hassfjell-Hoff’s system includes a gate valve that is used to selectively fluidly couple or isolate the source (when it is retracted into the upper chamber) and the lower volume (*i.e.*, lower collection chamber).

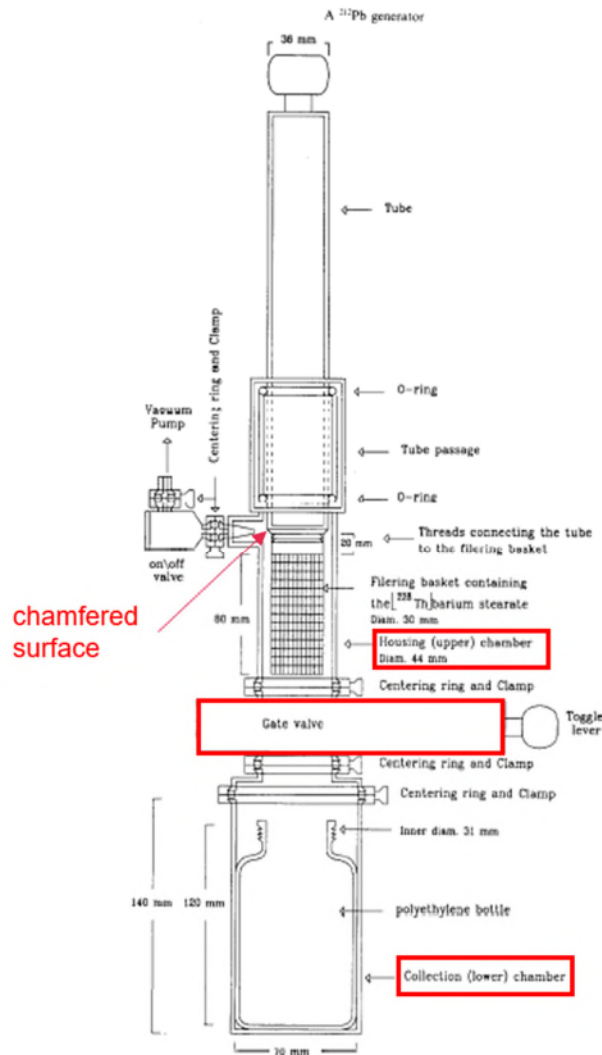


Fig. 2. The design of the generator showing functional details and operating mechanism.

EX1003, Fig. 2. Hassfjell-Hoff's system is designed to have a *gas tight seal*.

EX1003, 6 ("It therefore appeared to be a simpler and better approach to collect ^{212}Pb and ^{212}Bi by enclosing the $[\text{}^{228}\text{Th}]\text{barium stearate}$ in a gas-tight collection chamber."). Hassfjell-Hoff's system includes a *collector surface* (i.e., the interior walls of the polyethylene bottle) in the lower chamber (i.e., the claimed *volume*).

EX1003, 7, Fig. 2. In use, the solid precursor isotope source is initially positioned

in the upper chamber, and the gate valve is then opened. EX1003, 7. In this position, the upper and lower volumes are enclosed in a gas-tight seal formed by the O-rings between the tube and tube passage and the three sets of centering rings and clamps between the lower collection chamber and the tube passage. EX1003, 6-7. Hassfjell-Hoff's source is configured to be fluidly coupled to the volume with a gas-tight seal because it is placed in a position where the solid precursor isotope source (*i.e.*, packet of [^{228}Th]barium stearate) is fluidly coupled to the lower volume when the gate valve is open. Hassfjell-Hoff therefore discloses that the gate valve forms a gas-tight seal between the upper and lower chambers to selectively establish fluid communication between the upper and lower chambers of the generator. EX1002, ¶56. EX1019, ¶¶29-38.

b. Third Construction

Additionally, Hassfjell-Hoff discloses this limitation according to the third construction provided above: that the system is configured to selectively couple, using a gas tight seal, a volume with the solid precursor isotope source and a volume with a collector surface. *See* §§III(D)(1), (2) (construction of “fluidly coupled” and limitation 1c third construction). The gate valve is a gas tight seal that is selectively fluidly coupling the solid precursor isotope source to the volume that includes a collector surface. When the (gas tight seal) gate valve is closed, the solid precursor isotope source is not fluidly coupled. When the (gas tight seal) gate

valve is open, the solid precursor isotope source is fluidly coupled. EX1002, ¶57.

EX1019, ¶¶29-38.

5. **[1d] “wherein the solid precursor isotope source and the collector surface are configured such that the one or more gaseous progeny isotopes deposit one or more solid progeny isotopes on the collector surface.”**

Hassfjell-Hoff discloses this limitation. Hassfjell-Hoff discloses that the *solid precursor isotope source (i.e., packet of [²²⁸Th]barium stearate) and the collector surface (i.e., the interior walls of the polyethylene bottle) are configured such that the one or more gaseous progeny isotopes (i.e., gaseous ²²⁰Rn) deposit one or more solid progeny isotopes (i.e., ²¹²Pb and ²¹²Bi) on the collector surface:*

When the tube is lowered, the filtering basket with the emanating [²²⁸Th]barium stearate becomes positioned inside the bottle. The decay products from the emanated ²²⁰Rn, ²¹²Pb and ²¹²Bi, deposit on the walls of the bottle. After an appropriate collection time, the tube is pulled up, placing the ²²⁸Th source in the upper compartment, and the gate valve is closed. The polyethylene bottle is then removed and the radioactivity easily washed off with a suitable solution.

EX1003, 7. Hassfjell-Hoff discloses that the filtering basket with the emanating [²²⁸Th]barium stearate becomes positioned inside the bottle such that gaseous ²²⁰Rn (a progeny isotope of ²²⁸Th) emanates from the source and solid progeny isotopes

(²¹²Pb and ²¹²Bi) are deposited on the interior walls of the bottle (*i.e.*, the collector surface). EX1002, ¶58. EX1019, ¶¶29-38.

C. Claim 3 “The radioisotope generator of claim 1, further comprising a valve associated with the solid precursor isotope source.”

Hassfjell-Hoff discloses claim 1. *See* §IV(B) (claim 1). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §III(D)(3) (“associated with” construction). Hassfjell-Hoff discloses “[a]fter an appropriate collection time, the tube is pulled up, placing the ²²⁸Th source in the upper compartment, and the gate valve is closed.” EX1003, 7. As shown in Figure 2, when the gate valve is closed, it separates the collection surface from the solid precursor isotope source. Because the function of Hassfjell-Hoff’s gate valve is to isolate the solid precursor isotope source before collection time, Hassfjell-Hoff’s gate valve is associated with the solid precursor isotope source.

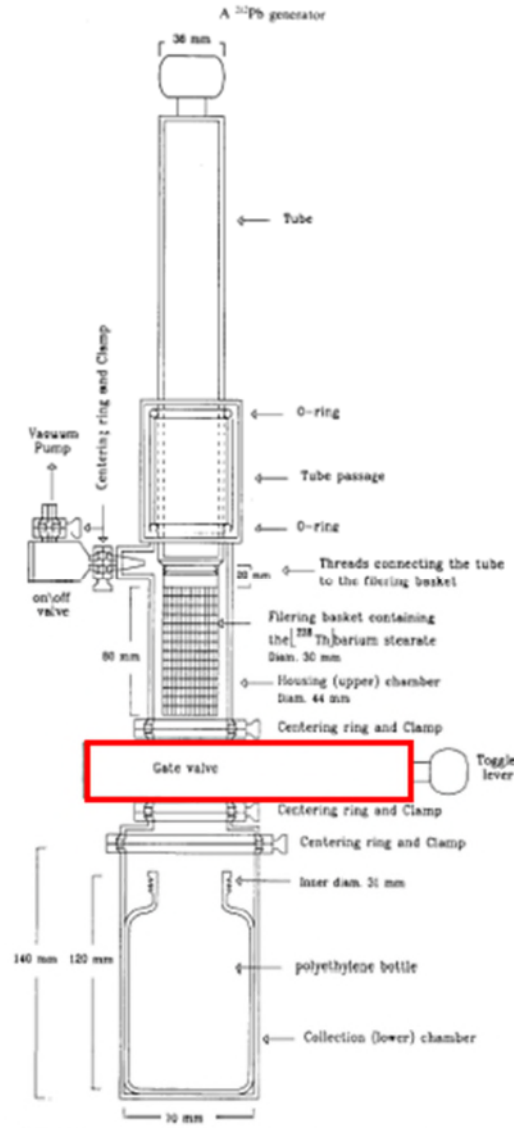


Fig. 2. The design of the generator showing functional details and operating mechanism

EX1003, Fig. 2. EX1002, ¶¶50-60. EX1019, ¶¶29-39.

D. Claim 4 “The radioisotope generator of claim 1, further comprising a vacuum pump attached to the volume.”

Hassfjell-Hoff discloses claim 1. See §IV(B) (claim 1). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Figure 2 of Hassfjell-Hoff depicts a vacuum pump attached to

the upper chamber, which is attached to the lower chamber (i.e., *volume*) via the gate valve:

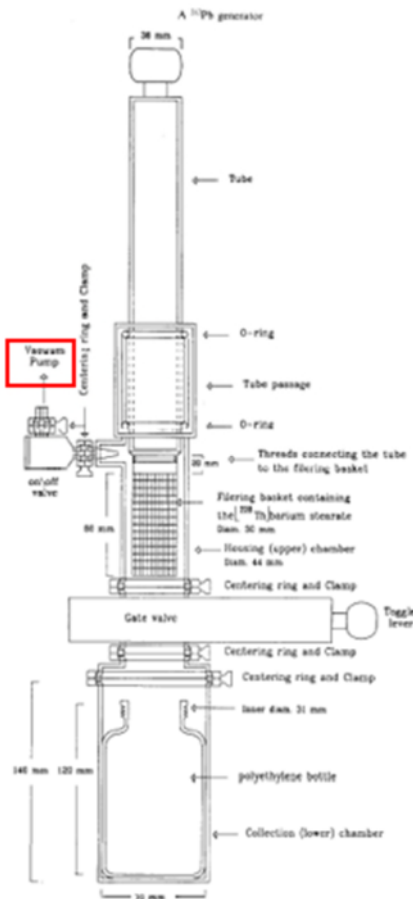


Fig. 2. The design of the generator showing functional details and operating mechanism.

EX1003, Fig. 2. Thus, Hassfjell-Hoff's vacuum pump is attached to the volume.

EX1002, ¶¶50-58, 61-62. EX1019, ¶¶29-38, 40.

- E. Claim 7 “The radioisotope generator of claim 1, wherein the precursor isotope comprises a thorium 228 isotope (^{228}Th) and/or a radium 224 isotope (^{224}Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (^{220}Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (^{212}Pb).”**

Hassfjell-Hoff discloses claim 1. See §IV(B) (claim 1). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Hassfjell-Hoff’s precursor isotope comprises ^{228}Th . EX1003, 7 (“When the tube is lowered, the filtering basket with the emanating [^{228}Th]barium stearate becomes positioned inside the bottle.”). Hassfjell-Hoff’s gaseous progeny isotope comprises ^{220}Rn . EX1003, 7 (“The decay products from the emanated ^{220}Rn ”). The solid progeny isotope comprises ^{212}Pb . EX1003, 7 (“ ^{212}Pb and ^{212}Bi , deposit on the walls of the bottle.”). Hassfjell-Hoff also discloses the overall decay chain from ^{228}Th to ^{224}Ra to ^{220}Rn to ^{216}Po to ^{212}Pb . EX1003, 7, Fig. 1. EX1002, ¶¶50-58, 63-64. EX1019, ¶¶29-38, 41

- F. Claim 8 “The radioisotope generator of claim 1, wherein the collector surface is an interior surface of a container, and wherein the volume is an internal volume of the container.”**

Hassfjell-Hoff discloses claim 1. See §IV(B) (claim 1). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. The collector surface is an interior surface of a container. See §IV(B)(4) (limitation 1c); EX1003, 7 (“The decay products from the emanated ^{220}Rn , ^{212}Pb and ^{212}Bi , deposit on the walls of the bottle.”). As explained above in

Section IV(B)(4) (limitation 1c), the internal volume of the container is fluidly coupled to the solid precursor isotope source. As shown above in Section IV(B)(4) (limitation 1c), Hassfjell-Hoff discloses a gas-tight seal the gate valve being a gas tight seal. EX1002, ¶¶50-58, 65-66. EX1019, ¶¶29-38, 42.

G. Claim 9 “The radioisotope generator of claim 8, wherein the solid precursor isotope source is configured to be connected to an opening of the container.”

Hassfjell-Hoff discloses claim 8. *See* §§IV(B), (F) (claims 1, 8). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §III(D)(4) (“connected to an opening of the container” construction). Figure 2 discloses that, based on the dimensions shown, *the solid precursor isotope source (i.e., packet of [²²⁸Th]barium stearate) is configured to be connected to an opening of the container:*

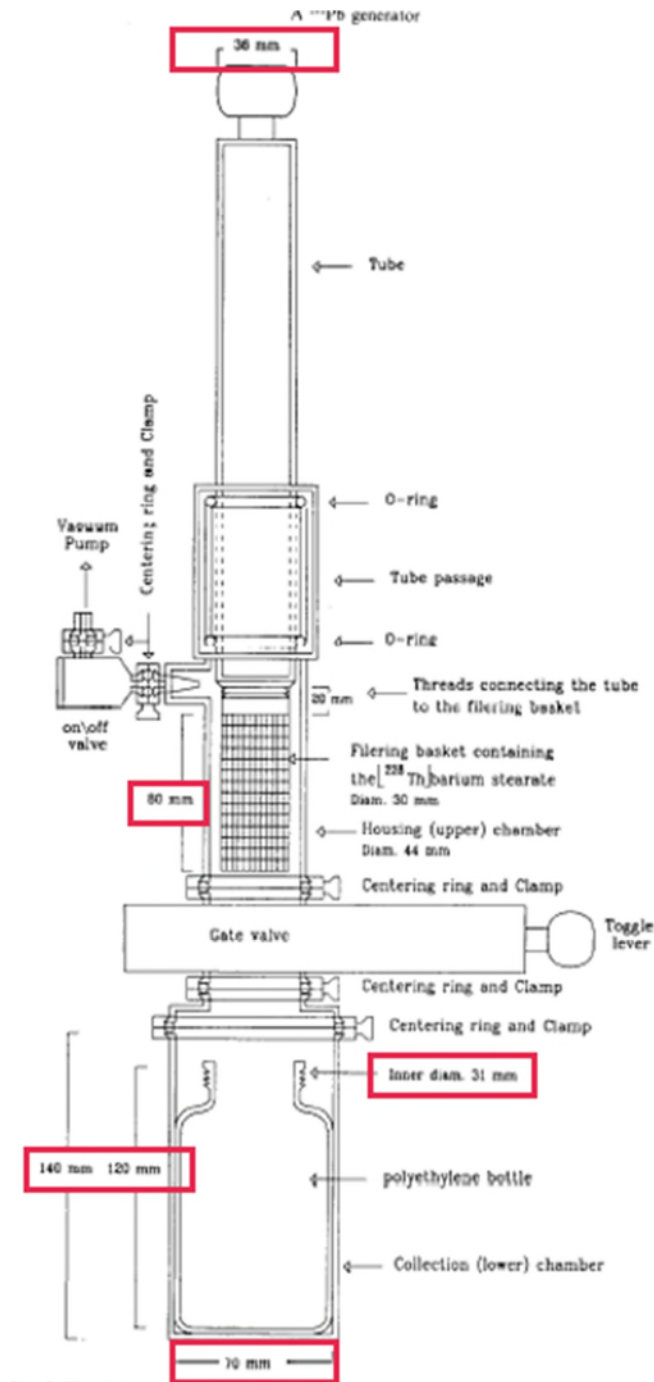


Fig. 2. The design of the generator showing functional details and operating mechanism.

EX1003, Fig. 2. Figure 2 of Hassfjell-Hoff depicts that the filing basket is connected to the tube (*i.e.*, rod) by threads. EX1003, Fig. 2. The threads are positioned at the bottom end of the tube. EX1003, Fig. 2. The tube has a diameter

of 36 mm. EX1003, Fig. 2. The inner diameter of the mouth of the polyethylene bottle is 31 mm. EX1003, Fig. 2. The filering basket containing the [²²⁸Th]barium stearate has a diameter of 30 mm and a height of 80 mm, and the polyethylene bottle has a height of 120 mm. EX1003, Fig. 2. The diameter of the filering basket (*i.e.*, 30 mm) is smaller than the inner diameter of the neck of the polyethylene bottle (*i.e.*, 31 mm). EX1003, Fig. 2. When the tube is pushed down to lower the filering basket, the tube slides on two O-rings, which are described in Figure 2 as “centering rings.” EX1003, Fig. 2. Based on these dimensions, a POSITA would have understood that the filering basket will be forced to stop being lowered by the neck of the bottle because the width of the tube (and threads) exceeds the width of the polyethylene bottle. EX1003, Fig. 2. Thus, the solid precursor isotope source in the filering basket is connected to the tube, and the tube (when pushed down) is connected to the opening of the bottle. EX1003, Fig. 2. Accordingly, a POSITA would have understood that a connection is formed between the solid precursor isotope source in the filering basket and the opening of the container when the tube contacts the neck of the polyethylene bottle. §III(D)(4) (“connected to an opening of the container” construction). EX1002, ¶¶50-58, 65-68. EX1019, ¶¶29-38, 42-43.

H. Claim 10 “The radioisotope generator of claim 8, further comprising the container.”

Hassfjell-Hoff discloses claim 8. See §§IV(B), (F) (claims 1, 8). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed

and in an enabling manner. The “polyethylene bottle” is a *container*. EX1003, Abstract, 7, Fig. 2. EX1002, ¶¶50-58, 65-66, 69-70. EX1019, ¶¶29-38, 42, 44.

I. Claim 11 “The radioisotope generator of claim 10, wherein the container is configured to removably connect to the solid precursor isotope source.”

Hassfjell-Hoff discloses claim 10. *See* §§IV(B), (F), (H) (claims 1, 8, 10). Hassfjell-Hoff further discloses the additional limitations of this claim as claimed and in an enabling manner. *See* §III(D)(5) (“removably connect” construction). As explained in reference to claim 9, the solid precursor isotope source is disclosed as being able to be connected and removed from a “polyethylene bottle” (i.e., *the container*). *See* §IV(G) (claim 9). EX1002, ¶¶50-58, 65-66, 69-72. EX1019, ¶¶29-38, 42, 44-45.

In addition, the container is disconnected from the solid precursor isotope source after an appropriate collection time when the filtering basket is withdrawn into the upper chamber. EX1003, 7 (“After an appropriate collection time, the tube is pulled up, placing the ²²⁸Th source in the upper compartment, and the gate valve is closed.”). As such, the container is configured to be *removably* connected to the solid precursor isotope source. EX1002, ¶¶50-58, 65-66, 69-73. EX1019, ¶¶29-38, 42, 44-45.

J. Claim 12 “The radioisotope generator of claim 10, further comprising a chelator disposed on the interior surface, the chelator configured to chelate the one or more solid progeny isotopes.”

Hassfjell-Hoff discloses claim 10. *See* §§IV(B), (F), (H) (claims 1, 8, 10).

Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. EX1003, 7 (“About 70% of the radioactivity inside the polyethylene bottle can be easily washed off with approx. 30 ml of distilled water. By increasing the ionic strength of the washing solution or by adding a chelating agent, the yield increases.”). EX1003, 7. The chelating agent (*i.e.*, the chelator) is disposed on the walls of the bottle (*i.e.*, when the interior surface is washed) and the chelating agent is configured to chelate the one or more solid progeny isotopes (*i.e.*, ^{212}Pb) from the interior surface. EX1002, ¶¶50-58, 65-66, 69-70, 74-75. EX1019, ¶¶29-38, 42, 44, 46.

K. Claim 14 “The radioisotope generator of claim 10, wherein the volume is configured to receive a solvent configured to dissolve the one or more solid progeny isotopes from the interior surface.”

Hassfjell-Hoff discloses claim 10. *See* §§IV(B), (F), (H) (claims 1, 8, 10).

Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Hassfjell-Hoff discloses *the volume* (*i.e.*, internal volume of the polyethylene container, *see* §IV(F) (claim 8)) *is configured to receive a solvent* (*e.g.*, water having a 1.0 M NaCl solution) *configured to dissolve the one or more solid progeny isotopes from the interior surface*. EX1003,

7 (“By increasing the ionic strength of the washing solution or by adding a chelating agent, the yield increases. With a 1.0 M NaCl, 99% of the ^{212}Pb can be washed of the walls of the bottle.”). The volume is configured to receive water having a 1.0 M NaCl solution (*i.e.*, a solvent) configured to dissolve the one or more solid progeny isotopes (*i.e.*, ^{212}Pb) from the interior walls of the container (*i.e.*, the interior surface). A POSITA would have understood that water having a 1.0 M NaCl solution would dissolve 99% of the solid progeny isotopes from the interior surface based on the disclosure of Hassfjell-Hoff. EX1003, 7. Similarly, a POSITA would understand that water itself will act as a solvent. Hassfjell-Hoff states “About 70% of the radioactivity inside the polyethylene bottle can be easily washed off with approx. 30 ml of distilled water”, and Norman similarly discloses that “the open porosity porous medium can be dissolved in water in order to obtain a solution whose principal radioactivity results from the daughter isotopes.” See EX1007, 4:1-4; EX1007, 4:47 (“solvent, such as water”). Ordinary water is also known to dissolve lead, which would include radioactive isotopes such as ^{212}Pb . See EX1016, 16-17 (describing a mechanism whereby chlorine ions in ordinary tap water will dissolve lead oxides in water pipes); EX1020. A POSITA would have understood that the progeny isotope is dissolved by the solvent when the porous medium, which contains the progeny isotope, is dissolved. EX1002, ¶¶50-58, 65-66, 69-70, 76-77. EX1019, ¶¶29-38, 42, 44, 47.

- L. Claim 15 “The radioisotope generator of claim 1, wherein the radioisotope generator is configured to be converted from a first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source, and a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source.”**

Hassfjell-Hoff discloses claim 1. See §IV(B) (claim 1). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Hassfjell-Hoff discloses the *radioisotope generator* has a *first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source*. EX1003, 7 (“the gate valve is closed.”), Fig. 1. As shown in Figure 1, when the gate valve is closed, the collector surface is not in fluid communication with the solid precursor isotope source because the two are in separate chambers separated by the gate valve. EX1003, Fig. 1, 7. Hassfjell-Hoff discloses converting from the first configuration (*i.e.*, opening the gate valve). See EX1003, 7. The radioisotope generator is also *configured to be converted from a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source*. See §IV(B)(4) (limitation 1c). Hassfjell-Hoff discloses converting from the second configuration (with the gate valve open) to the first configuration by closing the gate valve. EX1003, 7. EX1002, ¶¶50-58, 78-79. EX1019, ¶¶29-38, 48.

M. Claim 16

Hassfjell-Hoff discloses this claim arranged as claimed and in an enabling manner. EX1002, ¶¶80-86. EX1019, ¶¶29-38, 49.

1. [16pre] “A method of generating a progeny radioisotope, the method comprising:”

Hassfjell-Hoff discloses the preamble. See §IV(B)(1) (limitation 1pre).

Hassfjell-Hoff discloses a method of generating a progeny radioisotope using the depicted system. EX1003, 7. EX1002, ¶81. EX1019, ¶¶29-37, 49.

2. [16a] “allowing one or more gaseous progeny isotopes to emanate from a solid precursor isotope source”

Hassfjell-Hoff discloses this limitation. See §IV(B)(2) (limitation 1a).

Hassfjell-Hoff discloses *allowing one or more gaseous progeny isotopes (i.e., “Rn gas”) to emanate from a solid precursor isotope source (i.e., packet of [²²⁸Th]barium stearate):*

The packets of [²²⁸Th]barium stearate are placed in a filering basket mounted by threads to the end of a long tube closed in both ends. The filering basket has a capacity of 3-4 [²²⁸Th]barium stearate packets.... To collect the ²¹²Pb and ²¹²Bi, a polyethylene bottle is placed inside the collection chamber.

When the tube is lowered, the filering basket with the emanating [²²⁸Th]barium stearate becomes positioned inside the bottle. The decay products from the emanated ²²⁰Rn, ²¹²Pb and ²¹²Bi, deposit on the walls of the bottle.

EX1003, 7. EX1002, ¶82. EX1019, ¶¶29-38, 49.

3. [16b] “the solid precursor isotope source comprising a precursor isotope”

Hassfjell-Hoff discloses this limitation. See §IV(B)(3) (limitation 1b).

EX1002, ¶83. EX1019, ¶¶29-38, 49.

4. [16c] “fluidly coupling a volume including a collector surface to the solid precursor isotope source using a gas tight seal; and”

Hassfjell-Hoff discloses this limitation. Hassfjell-Hoff discloses *fluidly coupling a volume including a collector surface to the solid precursor isotope source using a gas tight seal* by opening the gate valve to connect the upper volume to the lower volume. See §IV(B)(4) (limitation 1c). EX1002, ¶84. EX1019, ¶¶29-38, 49.

Additionally, the gate valve is a gas tight seal that is selectively fluidly coupling the solid precursor isotope source to the volume that includes a collector surface. When the (gas tight seal) gate valve is closed, the solid precursor isotope source is not fluidly coupled. When the (gas tight seal) gate valve is open, the solid precursor isotope source is fluidly coupled. EX1002, ¶85. EX1019, ¶¶29-38, 49.

5. [16d] “allowing one or more solid progeny isotopes of the one or more gaseous progeny isotopes to deposit on the collector surface.”

Hassfjell-Hoff discloses this limitation. Hassfjell-Hoff discloses *allowing one or more solid progeny isotopes (i.e., ²¹²Pb) of the one or more gaseous*

progeny isotopes (i.e., ^{220}Rn) to deposit on the collector surface (i.e., walls of the polyethylene bottle). See §IV(B)(5) (limitation 1d). EX1002, ¶86. EX1019, ¶¶29-38, 49.

N. Claim 17 “The method of claim 16, further comprising flushing the collector surface.”

Hassfjell-Hoff discloses claim 16. See §IV(M) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. The interior surface of the polyethylene bottle (*i.e., collector surface*) is washed (*i.e., flushed*) to collect the progeny isotope. EX1003, 6 (“ ^{212}Pb deposits on the walls of a polyethylene bottle, and can be washed off with distilled water”), 7 (“The polyethylene bottle is then removed and the radioactivity easily washed off with a suitable solution.”). EX1002, ¶¶80-88. EX1019, ¶¶29-37, 49-50.

O. Claim 18 “The method of claim 16, wherein fluidly coupling the volume to the solid precursor isotope comprises opening a valve associated with the solid precursor isotope source.”

Hassfjell-Hoff discloses claim 16. See §IV(M) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(C) (claim 3). A POSITA would have understood that the gate valve is closed when the filtering basket is placed in the upper compartment, and that the gate valve must be opened to utilize the system. EX1003, 7. EX1002, ¶¶80-86, 89-90. EX1019, ¶¶29-37, 49, 51.

P. Claim 19 “The method of claim 16, further comprising drawing a vacuum in the volume.”

Hassfjell-Hoff discloses claim 16. See §IV(M) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim as claimed and in an enabling manner. Hassfjell-Hoff discloses that the vacuum pump of Figure 2 is attached to the volume. See §IV(D) (claim 4). The vacuum pump is disclosed as *drawing a vacuum in the volume*. EX1003, 7 (“The generator is shown in Figs 2 and 3. All generator parts...connected to standard high vacuum equipment to avoid leakage of radioactivity to the surroundings.”). Hassfjell-Hoff discloses utilizing the vacuum to decrease the pressure inside the volume, which a POSITA would have understood to disclose *drawing a vacuum in the volume*. EX1003, 7 (“The two compartments of the generator, one for collection and one for storage, combined with the possibility of decreasing the inside pressure, gives the generator a high degree of radiation safety.”). EX1002, ¶¶80-86, 91-92.

Q. Claim 22 “The method of claim 16, wherein the precursor isotope comprises a thorium 228 isotope (^{228}Th) and/or a radium 224 isotope (^{224}Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (^{220}Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (^{212}Pb).”

Hassfjell-Hoff discloses claim 16. See §IV(M) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(E) (claim 7). EX1002, ¶¶80-86, 93-94. EX1019, ¶¶29-37, 49, 52.

R. Claim 23 “The method of claim 16, wherein the collector surface is an interior surface of a container, and wherein the volume is an internal volume of the container.”

Hassfjell-Hoff discloses claim 16. *See* §IV(M) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(F) (claim 8). EX1002, ¶¶80-86, 95-96. EX1019, ¶¶29-37, 49, 53.

S. Claim 24 “The method of claim 23, further comprising connecting the solid precursor isotope source to an opening of the container.”

Hassfjell-Hoff discloses claim 23. *See* §§IV(M), (R) (claims 16, 23). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Hassfjell-Hoff discloses connecting the solid precursor isotope source to an opening of the container. *See* §§IV(G), (I) (claims 9, 11). EX1002, ¶¶80-86, 95-98. EX1019, ¶¶29-37, 49, 53-54.

T. Claim 25 “The method of claim 23, further comprising removably connecting the solid precursor isotope to an opening of the container.”

Hassfjell-Hoff discloses claim 23. *See* §§IV(M), (R) (claims 16, 23). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Hassfjell-Hoff discloses removably connecting the solid precursor isotope to an opening of the container. *See* §IV(I) (claim 11).

²²⁸Th is a solid precursor isotope disposed in the source. EX1003, 7 (“The desired

[²²⁸Th]barium stearate precipitated from the solution”). EX1002, ¶¶80-86, 95-96, 99-100. EX1019, ¶¶29-37, 49, 53, 55.

U. Claim 26 “The method of claim 23, further comprising chelating the one or more solid progeny isotopes using a chelator disposed on the interior surface.”

Hassfjell-Hoff discloses and claim 23. *See* §§IV(M), (R) (claims 16, 23).

Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(J) (claim 12); EX1003, 7 (“About 70% of the radioactivity inside the polyethylene bottle can be easily washed off with approx. 30 ml of distilled water. By increasing the ionic strength of the washing solution or by adding a *chelating agent*, the yield increases.”). EX1002, ¶¶80-86, 95-96, 101-102. EX1019, ¶¶29-37, 49, 53, 56.

V. Claim 28 “The method of claim 23, further comprising receiving a solvent in the volume, and dissolving the one or more solid progeny isotopes from the interior surface in the solvent.”

Hassfjell-Hoff discloses claim 23. *See* §§IV(M), (R) (claims 16, 23).

Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(K) (claim 14). Hassfjell-Hoff discloses that distilled water is received within the volume defined by the polyethylene bottle. EX1003, 7 (“About 70% of the radioactivity inside the polyethylene bottle can be easily washed off with approx. 30 ml of distilled water.”). A POSITA would have known that distilled water is a solvent used to

dissolve the solid progeny isotopes from the interior surface. See §IV(K) (claim 14). EX1002, ¶¶80-86, 95-96, 103-104. EX1019, ¶¶29-37, 49, 53, 57.

W. Claim 29 “The method of claim 16, wherein fluidly coupling the volume to the solid precursor isotope source comprises converting a radioisotope generator from a first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source to a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source.”

Hassfjell-Hoff discloses claim 16. See §IV(M) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(L) (claim 15). Hassfjell-Hoff’s radioisotope generator is configured to be converted from a first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source (*i.e.*, the gate valve is closed) to a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source (*i.e.*, with the gate valve open). EX1003, 7; §IV(L) (claim 15). EX1002, ¶¶80-86, 105-106. EX1019, ¶¶29-37, 49, 58.

X. Claim 31 “The method of claim 18, further comprising closing the valve to isolate the volume from the solid precursor isotope source.”

Hassfjell-Hoff discloses claim 18. See §§IV(M), (O) (claims 16, 18). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Hassfjell-Hoff discloses closing the valve to

isolate the volume from the solid precursor isotope source. EX1003, 7 (“After an appropriate collection time, the tube is pulled up, placing the ^{228}Th source in the upper compartment, and the gate valve is closed.”). A POSITA would have understood that closing the gate valve after the tube is pulled up isolates the volume from the solid precursor isotope source. EX1002, ¶¶80-86, 89-90, 107-108. EX1019, ¶¶29-37, 49, 51, 59.

Y. Claim 32 “The method of claim 16, wherein the solid precursor isotope is bound to a non-radioactive material.”

Hassfjell-Hoff discloses claim 16. See §IV(M) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. ^{228}Th is a solid precursor isotope disposed in the source. EX1003, 7 (“The desired [^{228}Th]barium stearate precipitated from the solution”). The solid precursor isotope is bound to a filter membrane, which a POSITA would have understood is a *non-radioactive material*. EX1003, 7 (“The desired [^{228}Th]barium stearate precipitated from the solution was filtered onto a 0.8 μm filter membrane (Gelman, U.S.), and washed with 25 ml of 100% methanol. The filter membrane was folded and wrapped up in two additional filters to avoid any loss of [^{228}Th]barium stearate.”). A POSITA would have understood “Gelman, U.S.” to refer to a well-known supplier of non-radioactive filter membranes. For example, Bhagwatwar discloses that Gelman filter membranes (used in the same way as practiced by Hassfjell-Hoff) were made from 0.2 μm nylon 66 sterilizing

grade. *See* EX1012, [0014], [0041], [0047]-[0049]. Nylon 66 is non-radioactive because it is a linear polyamide that does not include any radioactive compounds. EX1013, cl. 8 (showing the chemical formula of nylon 66 does not include any radioactive atoms or compounds). EX1002, ¶¶80-86, 109-110. EX1019, ¶¶29-37, 49, 60-61.

Z. Claim 34 “The method of claim 23, forming at least a portion of a single chamber with the solid precursor isotope source and the container.”

Hassfjell-Hoff discloses claim 23. *See* §§IV(M, R) (claims 16, 23).

This claim is indefinite. *See* §XIV(C). To the extent Patent Owner argues that this claim should be construed to require “[t]he method of claim 23, **further comprising,**” Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner,. *See* §III(D)(6) (“with” construction). Hassfjell-Hoff’s system includes a gate valve that opens/closes, such that when it is opened there is a *single chamber* that includes *the solid precursor isotope source and the container*. EX1003, 7, Fig. 2. When the gate valve is closed there are two separate chambers, the lower and upper chambers. Thus, opening the gate valve *form[s]...a single chamber*. EX1003, 7. EX1002, ¶¶80-86, 95-96, 111-113. EX1019, ¶¶29-37, 49, 53, 62.

AA. Claim 35 “The radioisotope generator of claim 3, wherein the valve is configured to isolate the solid precursor isotope from the volume in a closed position.”

Hassfjell-Hoff discloses claim 3. See §§IV(B)-(C) (claims 1, 3). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner because it discloses *the valve (i.e., gate valve) is configured to isolate the solid precursor isotope from the volume in a closed position* (i.e., when closed, the gate valve isolates the solid precursor isotope from the container). See §IV(X) (claim 31). EX1002, ¶¶50-60, 114-115. EX1019, ¶¶29-39, 63.

BB. Claim 36 “The radioisotope generator of claim 1, wherein the solid precursor isotope is bound to a non-radioactive material.”

Hassfjell-Hoff discloses claim 1. See §IV(B) (claim 1). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(Y) (claim 32). ^{228}Th is a solid precursor isotope disposed in the source. EX1003, 7 (“The desired [^{228}Th]barium stearate precipitated from the solution”). The solid precursor isotope is bound to a filter membrane, which a POSITA would have understood is a *non-radioactive material*. See §IV(Y) (claim 32). EX1002, ¶¶50-58, 116-117. EX1019, ¶¶29-38, 64-65.

CC. Claim 38 “The radioisotope generator of claim 10, wherein the solid precursor isotope source and the container form at least a portion of a single chamber when fluidly coupled.”

Hassfjell-Hoff discloses claim 10. *See* §§IV(B), (F), (H) (claims 1, 8, 10).

Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(Z) (claim 34). EX1002, ¶¶50-58, 65-66, 69-70, 118-119. EX1019, ¶¶29-38, 42, 44, 66.

V. GROUND 2: CLAIMS 1, 3-4, 7-12, 14-19, 22-26, 28-29, 31-32, 34-36, AND 38 ARE RENDERED OBVIOUS BY HASSFJELL-HOFF

A. Hassfjell-Hoff

See §IV(A). EX1002, ¶¶44-49. EX1019, ¶¶29-33

B. Claim 1

Hassfjell-Hoff renders this claim obvious. EX1002, ¶¶44-49.

1. [1pre] “A radioisotope generator comprising:”
 - [1a] “a solid precursor isotope source configured to emanate one or more gaseous progeny isotopes”
 - [1b] “the solid precursor isotope source comprising a precursor isotope; and
 -
 - [1d] “wherein the solid precursor isotope source and the collector surface are configured such that the one or more gaseous progeny isotopes deposit one or more solid progeny isotopes on the collector surface.”

Hassfjell-Hoff discloses these limitations. *See* §§IV(B)(1)-(3), (5)

(limitations 1pre, 1a, 1b, 1d). EX1002, ¶¶50-54, 58.

2. [1c] “wherein the solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface with a gas tight seal, and”

As explained above, this limitation is disclosed by Hassfjell-Hoff (§IV(B)(4) (limitation 1c)) under the first and third constructions. *See* §§III(D)(1), (2) (construction of “fluidly coupled” and limitation 1c first and third constructions). EX1002, ¶55.

If Patent Owner argues, incorrectly, that Hassfjell-Hoff’s gate valve does not form a gas-tight seal, it would have been obvious to implement Hassfjell-Hoff’s gate-valve as establishing a gas-tight seal between the upper and lower collection chambers. A POSITA would have been motivated and found it obvious to implement the gate valve to be a gas-tight seal. Gas-tight gate valves for sealing harmful gases that can cause damage were well-known in the art, and a POSITA would have been motivated to use one for the gate valve in Hassfjell-Hoff for user safety when replacing the polyethene bottle. For example, Ishigaki discloses a gate valve that minimizes the chance that compounds in exhaust gas will contact a main valve seal. EX1018, Cover. A POSITA would have been motivated to configure the Hassfjell-Hoff system to form a gas-tight seal to enhance safety for the worker performing collection, and would have had a reasonable expectation of success because such gas-tight seals are well-known. EX1002, ¶56.

C. Claims 3-4, 7-12, 14-15, 35-36, and 38

As explained above, Hassfjell-Hoff renders obvious claim 1. *See* §V(B) (claim 1). As explained above, the additional limitations of these claims are disclosed by Hassfjell-Hoff. *See* §§IV(C)-(L), (AA)-(CC) (claims 3-4, 7-12, 14-15, 35-36, 38). Therefore, these claims are rendered obvious by Hassfjell-Hoff.

EX1002, ¶¶50-79, 114-119. EX1019, ¶¶29-38, 42, 44, 47, 67, 71-72.

D. Claim 16

Hassfjell-Hoff discloses and renders this claim obvious. *See* §V(B); §IV(M). EX1002, ¶¶80-86.

E. Claims 17-19, 22-26, 28-29, 31-32, and 34

As explained above, Hassfjell-Hoff renders obvious claim 16. *See* §V(D) (claim 16). As explained above, the additional limitations of these claims are disclosed by Hassfjell-Hoff. *See* §§IV(N)-(Z) (claims 17-19, 22-26, 28-29, 31-32, 34). Therefore, these claims are rendered obvious by Hassfjell-Hoff. EX1002, ¶¶80-113. EX1019, ¶¶29-37, 49, 53-54, 68-70.

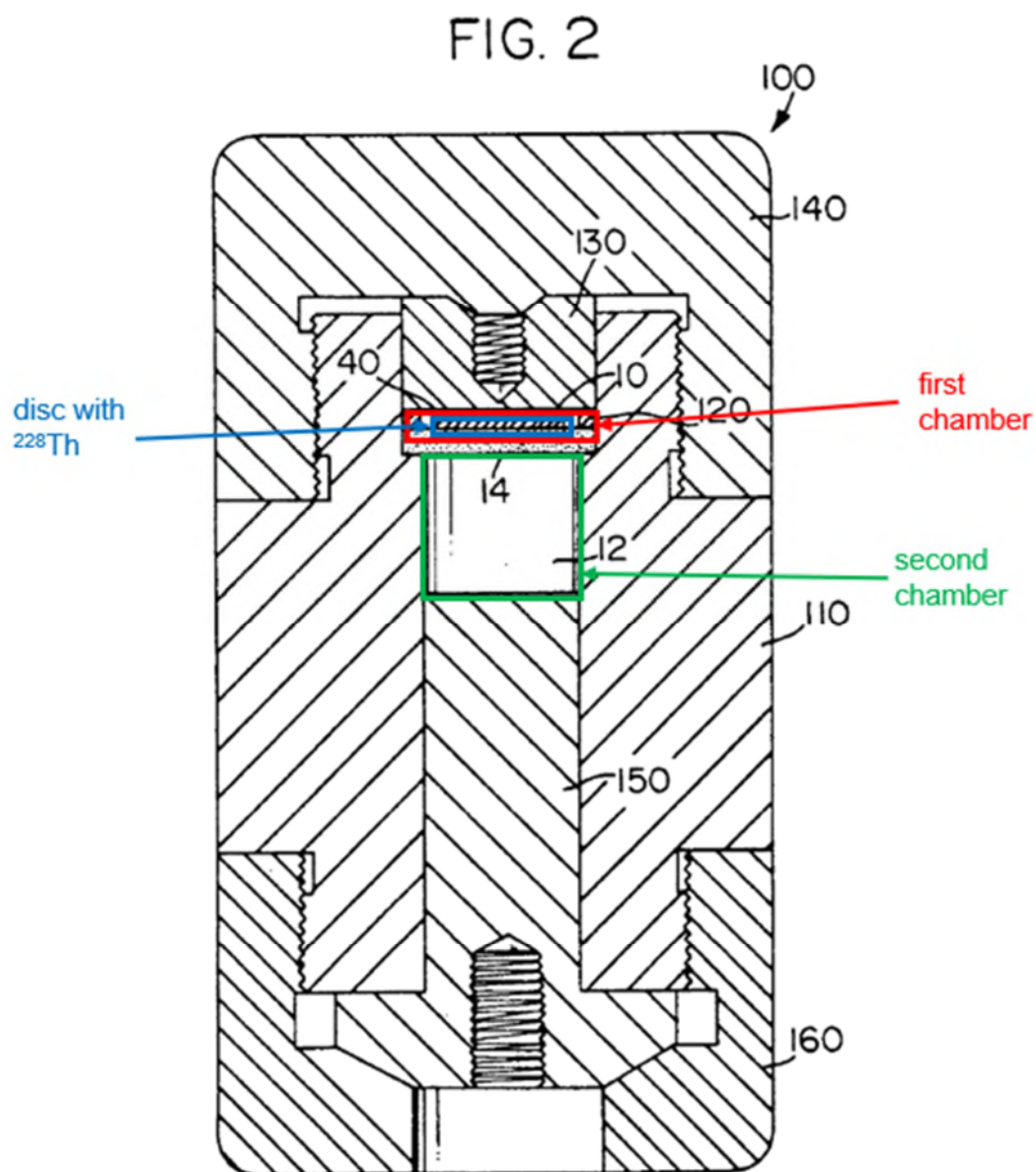
VI. GROUND 3: CLAIMS 1, 3, 5-7, 15-16, 18, 20-22, 29-33, AND 35-37 ARE ANTICIPATED BY NORMAN

A. Norman

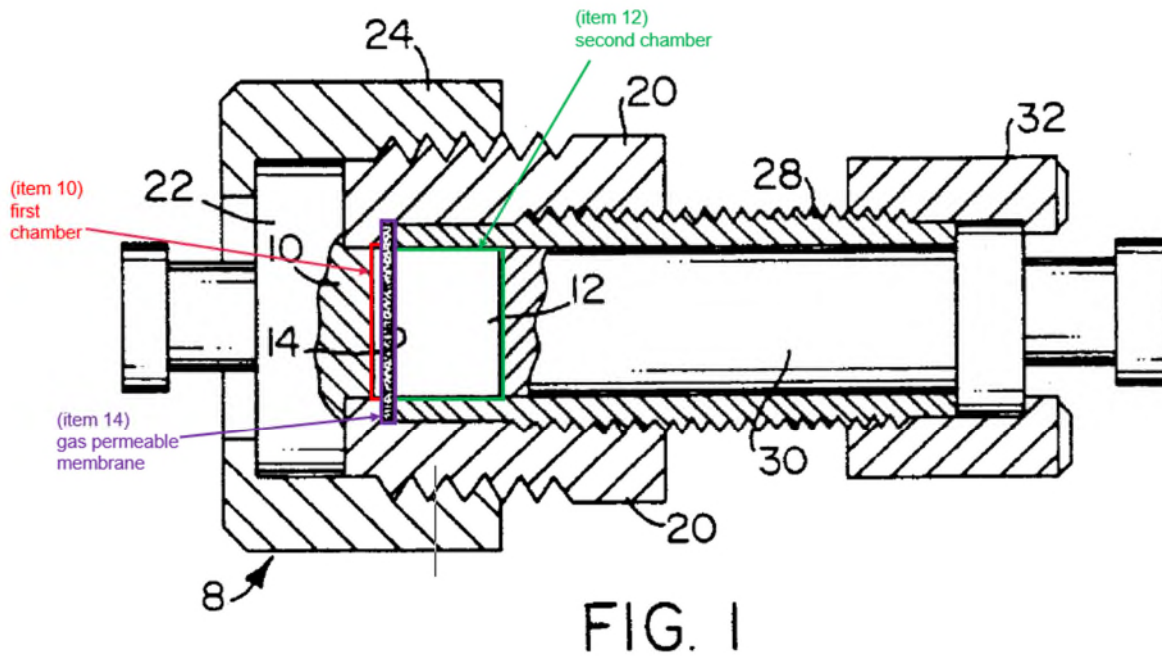
United States Patent No. 5,038,046 to Norman et al. (“Norman”) was filed on July 10, 1990 and issued on August 6, 1991. EX1007, 1. As such, Norman was published and available to the public no later than August 6, 1991. EX1007, 1.

Norman qualifies as prior art under (AIA) 35 U.S.C. §102(a). Because Norman was published and available to the public no later than August 6, 1991, which is more than 1 year before the effective filing date of the 437 patent, the (post-AIA) 35 U.S.C. §102(b) exceptions do not apply. EX1002, ¶120.

Norman discloses a method and generator for preparing the radioisotope of lead, ^{212}Pb , whereby ^{228}Th , in a closed first chamber 10, is allowed to decay to gaseous ^{220}Rn which is then readily separated from the thorium and other decay products by diffusing the ^{220}Rn gas into a second chamber 12, where it decays to ^{212}Pb which can then be collected from the second chamber. *See* EX1007, Abstract.



EX1007, Fig. 2.



EX1007, Fig. 1. Figures 1 and 2 are each an “alternate embodiment of the generator.” EX1007, 2:40-45, 7:65-8:1. EX1002, ¶121.

Norman is analogous art to the 437 patent. EX1001; EX1006. Moreover, as shown below, it was a material error for certain claims of the 437 patent to issue over Norman. EX1002, ¶¶122-123.

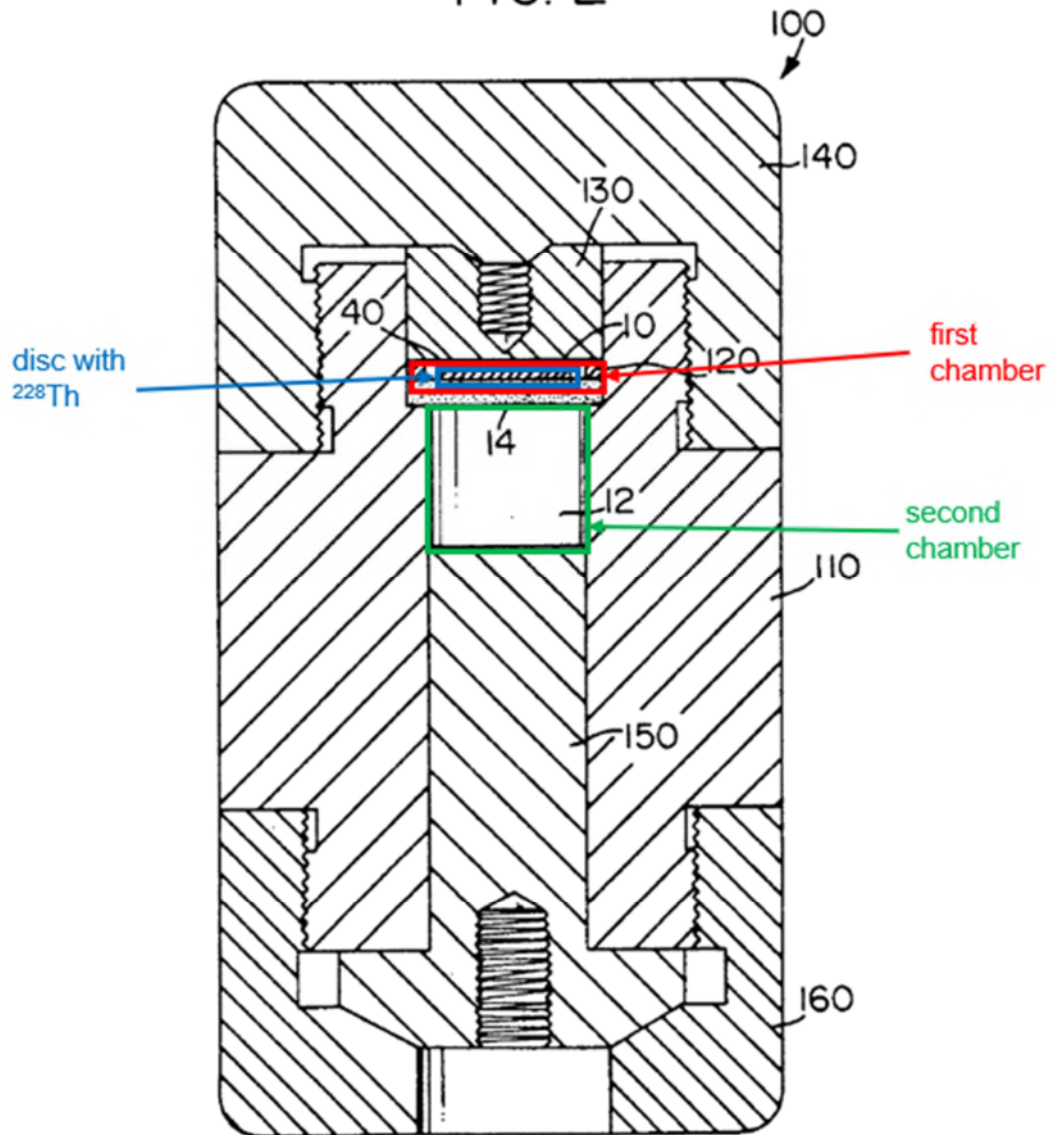
B. Claim 1

Norman discloses this claim arranged as claimed and in an enabling manner. EX1002, ¶¶124-131, 133-134.

1. [1pre] “A radioisotope generator comprising:”

Norman discloses the preamble. EX1007, Abstract (“A method and generator for preparing the radioisotope of lead, ^{212}Pb ”).

FIG. 2



EX1007, Fig. 2. EX1002, ¶125.

2. [1a] “a solid precursor isotope source configured to emanate one or more gaseous progeny isotopes”

Norman discloses this limitation. The combination of the ^{228}Th in a matrix, is a *solid precursor isotope source*. EX1007, 3:53-56 (“ ^{228}Th compounds can be

ground into super fine particles which are dispersed into a matrix”). Norman discloses that the matrix is a solid. EX1007, 3:53-56 (“graphite particles, alumina, and inert ceramic”). The ^{228}Th in the matrix is *configured to emanate one or more gaseous progeny isotopes*. EX1007, Abstract (“ ^{228}Th , in a closed chamber, is allowed to decay into gaseous ^{220}Rn which is then readily separated from the thorium and other decay products by diffusing the ^{220}Rn gas into a second chamber”). EX1002, ¶126.

3. [1b] “the solid precursor isotope source comprising a precursor isotope; and”

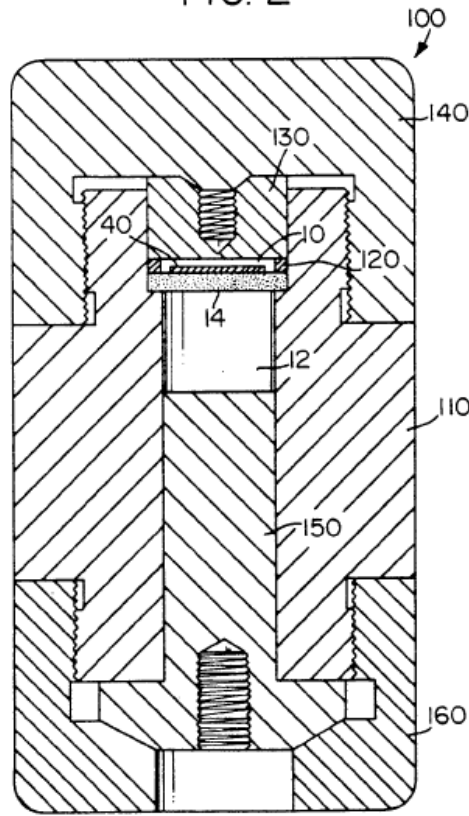
Norman discloses this limitation. The combination of the ^{228}Th in a matrix, (i.e., *solid precursor isotope source*) includes the precursor isotope ^{228}Th . See §VI(B)(2) (limitation 1a). EX1002, ¶127.

4. [1c] “wherein the solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface using a gas tight seal, and”

a. First and Second Constructions

Norman discloses this limitation under either the first or second constructions of limitation 1c. See §§III(D)(1), (2) (constructions of “fluidly coupled” and limitation 1c). As shown in Figure 2, the solid precursor isotope source 40 is fluidly coupled to the second chamber 12 (a *volume*) through gas permeable membrane 14.

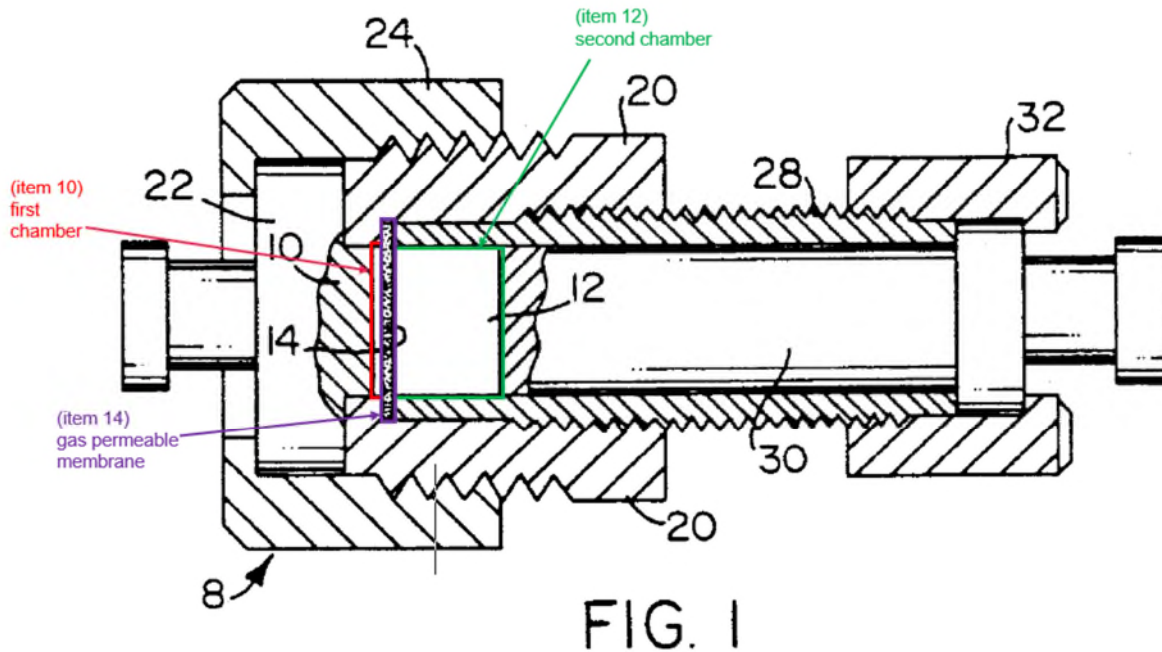
FIG. 2



EX1007, Fig. 2, 6:12-21 (“the generator comprises a parental chamber 10, a receiving chamber 12, and a gas elute means such as gas permeable membrane 14 interposed between and separating the two chambers 10 and 12. The gas permeable membrane 14 must have a pore size sufficient to permit the rapid diffusion of the gaseous intermediary therethrough while, at the same time, preventing the parent isotope from passing into receiving chamber 12.”).

Norman’s embodiment in Figure 1 discloses a *solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface using a gas tight seal*. EX1007, 7:22-25 (“If the receiving chamber is also closed,

i.e., both plungers 22 and 30 are inserted and secured with end caps 24 and 32, the escape of radon from the generator is prevented.”).



EX1007, Fig. 1. EX1002, ¶¶128-129.

Norman discloses a collector surface is the sides of the collecting chamber 12. EX1007, 3:8-11 (“Decay of ^{220}Rn to ^{212}Pb (via very short lived polonium-216) causes recoils which tend to embed the lead in the open porosity porous medium **as well as in any other solid exposed to the radon.**”). Alternatively, Norman discloses that the collector surface is a porous medium. EX1007, 3:4-20. EX1002, ¶130.

A POSITA would have understood that Norman discloses that the embodiment of Figure 2 has the solid precursor isotope source (i.e., ^{228}Th

encapsulated in a matrix) configured to be fluidly coupled to a volume including a collector surface (via the gas permeable membrane 14) using a gas tight seal (*i.e.*, by which the escape of radon from the generator is prevented). EX1007, 7:65-8:24 (discussing various “seal” elements in figure 2), Fig. 2. EX1002, ¶131.

b. Third Construction

Additionally, Norman discloses this limitation according to the third construction provided above: that the system is configured to selectively couple, using a gas tight seal, a volume with the solid precursor isotope source and a volume with a collector surface. *See* §§III(D)(1), (2) (construction of “fluidly coupled” and limitation 1c third construction). Norman’s stopcock is a gas tight seal that is selectively fluidly coupling the solid precursor isotope source to the volume that includes a collector surface. Norman discloses using a stopcock (*i.e.*, valve) that can be opened to allow the solid precursor isotope source to emanate gaseous progeny isotopes from the first chamber 10 to the second chamber 12. EX1007, 8:33-41 (“it is apparent that the reactor could be designed such that the two chambers are physically separated from each other and connected by a passageway through which the gaseous product could diffuse without permitting transfer of any solid material, *e.g.*, a stopcock. Thus, when the stopcock is opened, the gaseous ²²⁰Rn diffuses from parental chamber 10 into the collection chamber 12.”). When the (gas tight seal) stopcock is closed, the solid precursor isotope

source is not fluidly coupled. When the (gas tight seal) stopcock is open, the solid precursor isotope source is fluidly coupled. EX1002, ¶133.

5. **[1d] “wherein the solid precursor isotope source and the collector surface are configured such that the one or more gaseous progeny isotopes deposit one or more solid progeny isotopes on the collector surface.”**

Norman discloses this limitation. EX1007, Abstract (“A method and generator for preparing the radioisotope of lead, ^{212}Pb , whereby ^{228}Th , in a closed chamber, is allowed to decay to gaseous ^{220}Rn which is then readily separated from the thorium and other decay products by diffusing the ^{220}Rn gas into a second chamber, where it decays to ^{212}Pb which can then be collected from the second chamber.”), 2:65-3:11 (“the process and generator of the present invention involve the decay of a parent isotope, such as ^{228}Th , within a first closed chamber to yield a gaseous decay product, such as ^{220}Rn ...Decay of ^{220}Rn to ^{212}Pb (via very short lived polonium-216) causes recoils which tend to embed the lead in the open porosity porous medium as well as in any other solid exposed to the radon.”). EX1002, ¶134.

C. **Claim 3 “The radioisotope generator of claim 1, further comprising a valve associated with the solid precursor isotope source.”**

Norman discloses claim 1. See §VI(B) (claim 1). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §III(D)(3) (“associated with” construction). Norman discloses using a

stopcock (*i.e.*, valve) that can be opened to allow the solid precursor isotope source to emanate gaseous progeny isotopes from the first chamber 10 to the second chamber 12. EX1007, 8:33-41 (“it is apparent that the reactor could be designed such that the two chambers are physically separated from each other and connected by a passageway through which the gaseous product could diffuse without permitting transfer of any solid material, *e.g.*, a stopcock. Thus, when the stopcock is opened, the gaseous ^{220}Rn diffuses from parental chamber 10 into the collection chamber 12.”). EX1002, ¶¶124-131, 133-136.

D. Claim 5 “The radioisotope generator of claim 1, wherein the solid precursor isotope source comprises a porous material configured to retain the precursor isotope.”

Norman discloses claim 1. *See* §VI(B) (claim 1). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. The *solid precursor isotope source* (*i.e.*, ^{228}Th in the matrix) *comprises a porous material* (*e.g.*, “inert materials...form...a porous matrix”) *configured to retain the precursor isotope*. EX1007, 7:60-64 (“Other inert materials which allow free diffusion of the ^{220}Rn gas therethrough and are not subject to important decomposition by radiation may be used to form such a porous matrix for the ^{228}Th , including but not limited to alumina and inert ceramic.”). EX1002, ¶¶124-131, 133-134, 137-138.

E. Claim 6 “The radioisotope generator of claim 5, wherein the precursor isotope is absorbed, adsorbed, and/or encapsulated by the porous material.”

Norman discloses claim 5. See §§VI(B), (D) (claims 1, 5). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman discloses that *the precursor isotope is...encapsulated by the porous material*. EX1007, 7:51-56 (“super fine particles of ^{228}Th are dispersed within a porous matrix, such as, for example, similarly powdered graphite, that will not absorb the ^{220}Rn gas. The mixture can be compacted so that the ^{228}Th is encapsulated within the graphite and forms a graphite disc 40 as shown in FIG. 2.”). EX1002, ¶¶124-131, 133-134, 137-140.

F. Claim 7 “The radioisotope generator of claim 1, wherein the precursor isotope comprises a thorium 228 isotope (^{228}Th) and/or a radium 224 isotope (^{224}Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (^{220}Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (^{212}Pb).”

Norman discloses claim 1. See §VI(B) (claim 1). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. EX1007, Abstract (“A method and generator for preparing the radioisotope of lead, ^{212}Pb , whereby ^{228}Th , in a closed chamber, is allowed to decay to gaseous ^{220}Rn which is then readily separated from the thorium and other decay products by diffusing the ^{220}Rn gas into a second chamber, where it decays to ^{212}Pb

which can then be collected from the second chamber.”). EX1002, ¶¶124-131, 133-134, 141-142.

G. Claim 15 “The radioisotope generator of claim 1, wherein the radioisotope generator is configured to be converted from a first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source, and a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source.”

Norman discloses claim 1. *See* §VI(B) (claim 1). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman’s stopcock allows the generator to be converted from *a first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source, and a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source*. EX1007, 8:33-41 (“it is apparent that the reactor could be designed such that the two chambers are physically separated from each other and connected by a passageway through which the gaseous product could diffuse without permitting transfer of any solid material, e.g., a stopcock. Thus, when the stopcock is opened, the gaseous ²²⁰Rn diffuses from parental chamber 10 into the collection chamber 12.”). EX1002, ¶¶124-131, 133-134, 143-144.

H. Claim 16

Norman discloses this claim arranged as claimed and in an enabling manner. EX1002, ¶¶145-150.

1. [16pre] “A method of generating a progeny radioisotope, the method comprising:”

Norman discloses the preamble. See §VI(B)(1) (limitation 1pre). Norman discloses a method of generating a progeny radioisotope using the depicted system. EX1007, Abstract (“A method and generator for preparing the radioisotope of lead, ^{212}Pb , whereby ^{228}Th , in a closed chamber, is allowed to decay to gaseous ^{220}Rn which is then readily separated from the thorium and other decay products by diffusing the ^{220}Rn gas into a second chamber, where it decays to ^{212}Pb which can then be collected from the second chamber.”). EX1002, ¶146.

2. [16a] “allowing one or more gaseous progeny isotopes to emanate from a solid precursor isotope source”

Norman discloses this limitation. See §VI(B)(2) (limitation 1a). EX1007, Abstract (“ ^{228}Th , in a closed chamber, is allowed to decay into gaseous ^{220}Rn which is then readily separated from the thorium and other decay products by diffusing the ^{220}Rn gas into a second chamber.”). EX1002, ¶147.

3. [16b] “the solid precursor isotope source comprising a precursor isotope”

Norman discloses this limitation. See §VI(B)(3) (limitation 1b). EX1002, ¶148.

4. **[16c] “fluidly coupling a volume including a collector surface to the solid precursor isotope source using a gas tight seal; and”**

Norman discloses this limitation. See §VI(B)(4) (limitation 1c). EX1002, ¶149.

5. **[16d] “allowing one or more solid progeny isotopes of the one or more gaseous progeny isotopes to deposit on the collector surface.”**

Norman discloses this limitation. See §VI(B)(5) (limitation 1d). EX1002, ¶150.

- I. **Claim 18 “The method of claim 16, wherein fluidly coupling the volume to the solid precursor isotope comprises opening a valve associated with the solid precursor isotope source.”**

Norman discloses claim 16. See §VI(H) (claim 16). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman discloses *fluidly coupling the volume to the solid precursor isotope comprises opening a valve (i.e., “stopcock”) associated with the solid precursor isotope source*. EX1007, 8:33-41; §VI(C) (claim 3). EX1002, ¶¶145-152.

- J. **Claim 20 “The method of claim 16, wherein the solid precursor isotope source comprises a porous material configured to retain the precursor isotope.”**

Norman discloses claim 16. See §VI(H) (claim 16). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §VI(D) (claim 5). EX1002, ¶¶145-150, 153-154.

K. Claim 21 “The method of claim 20, wherein the precursor isotope is absorbed, adsorbed, and/or encapsulated by the porous material.”

Norman discloses claim 20. See §VI(H), (J) (claims 16, 20). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §VI(E) (claim 6); EX1007, 7:51-56. EX1002, ¶¶145-150, 153-156.

L. Claim 22 “The method of claim 16, wherein the precursor isotope comprises a thorium 228 isotope (^{228}Th) and/or a radium 224 isotope (^{224}Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (^{220}Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (^{212}Pb).”

Norman discloses claim 16. See §VI(H) (claim 16). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §VI(F) (claim 7). EX1007, Abstract. EX1002, ¶¶145-150, 157-158.

M. Claim 29 “The method of claim 16, wherein fluidly coupling the volume to the solid precursor isotope source comprises converting a radioisotope generator from a first configuration in which the collector surface is not in fluid communication with the solid precursor isotope source to a second configuration in which the collector surface is in fluid communication with the solid precursor isotope source.”

Norman discloses claim 16. See §VI(H) (claim 16). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §VI(G) (claim 15). EX1007, 8:33-41. EX1002, ¶¶145-150, 159-160.

N. Claim 30 “The method of claim 16, further comprising forming a radiopharmaceutical using the one or more solid progeny isotopes.”

Norman discloses claim 16. See §VI(H) (claim 16). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. A POSITA would have understood that Norman discloses using a radioisotope generator to *form[] a radiopharmaceutical using...solid progeny isotopes*. EX1007, Abstract (“The ²¹²Pb can be recovered from this medium by dissolving the medium or by reacting it with an antibody-chelating complex solution to entrap it in the antibody-chelating complex”), 1:17-24 (“Radiation therapy has long been used in the treatment of cancer and other localized lesions. The development of monoclonal antibodies, which can be targeted to specific cells with a high degree of specificity, has made it possible to selectively deliver radioactive agents predominantly to specifically targeted cells. The choice of an appropriate radioactive isotope is the critical aspect in targeting radiation therapy.”). EX1002, ¶¶145-150, 161-162.

O. Claim 31 “The method of claim 18, further comprising closing the valve to isolate the volume from the solid precursor isotope source.”

Norman discloses claim 18. See §§VI(H)-(I) (claims 16, 18). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman discloses closing the valve (*i.e.*, “stopcock”) to isolate

the volume from the solid precursor isotope source. EX1007, 8:33-41. EX1002, ¶¶145-152, 163-164.

P. Claim 32 “The method of claim 16, wherein the solid precursor isotope is bound to a non-radioactive material.”

Norman discloses claim 16. See §VI(H) (claim 16). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman discloses that the solid precursor isotope is bound to “inert ceramic,” which a POSITA would have understood to be a non-radioactive material. EX1007, 7:51-64. ²²⁸Th is a solid disposed in the matrix. See §VI(B)(3) (limitation 1b). EX1002, ¶ EX1002, ¶¶145-150, 165-166.

Q. Claim 33 “The method of claim 32, wherein the non-radioactive material is a ceramic.”

Norman discloses claim 32. See §§VI(H), (P) (claims 16, 32). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §VI(P) (claim 32). EX1007, 7:51-64. EX1002, ¶145-150, 165-168.

R. Claim 35 “The radioisotope generator of claim 3, wherein the valve is configured to isolate the solid precursor isotope from the volume in a closed position.”

Norman discloses claim 3. See §§VI(B)-(C) (claims 1, 3). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman discloses *the valve (i.e., stopcock) is configured to*

isolate the solid precursor isotope from the volume in a closed position. See

§VI(O) (claim 31). EX1002, ¶¶124-131, 133-136, 169-170.

S. Claim 36 “The radioisotope generator of claim 1, wherein the solid precursor isotope is bound to a non-radioactive material.”

Norman discloses claim 1. See §VI(B) (claim 1). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §VI(P) (claim 32). ²²⁸Th is a solid disposed in the matrix. See §VI(B)(3) (limitation 1b). EX1002, ¶¶124-131, 133-134, 171-172.

T. Claim 37 “The radioisotope generator of claim 36, wherein the non-radioactive material is a ceramic.”

Norman discloses claim 36. See §§VI(B), (S) (claims 1, 36). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §VI(Q) (claim 33). EX1002, ¶¶124-131, 133-134, 171-174.

VII. GROUND 4: CLAIMS 1, 3, 5-7, 15-16, 18, 20-22, 29-33, AND 35-37 ARE RENDERED OBVIOUS BY NORMAN

A. Norman

See §VI(A). EX1002, ¶¶120-123.

B. Claim 1

Norman renders this claim obvious. EX1002, ¶¶124-134.

1. **[1pre] “A radioisotope generator comprising:”**
[1a] “a solid precursor isotope source configured to emanate one or more gaseous progeny isotopes”
[1b] “the solid precursor isotope source comprising a precursor isotope; and
....
[1d] “wherein the solid precursor isotope source and the collector surface are configured such that the one or more gaseous progeny isotopes deposit one or more solid progeny isotopes on the collector surface.”

Norman discloses these limitations. *See* §§VI(B)(1)-(3), (5) (limitations 1pre, 1a, 1b, 1d). EX1002, ¶¶124-127, 134.

2. **[1c] “wherein the solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface with a gas tight seal, and”**

As explained above, this limitation is disclosed by Norman (§VI(B)(4) (limitation 1c)) under all constructions of limitation 1c. *See* §§III(D)(1), (2) (construction of “fluidly coupled” and limitation 1c construction). EX1002, ¶¶128-131, 133.

If Patent Owner argues, incorrectly, that Norman does not disclose that Figure 2 has a gas-tight seal, Norman renders obvious this limitation. It would have been obvious to a POSITA to utilize the teaching of Norman regarding having a gas tight seal for Figure 1 in the Figure 2 embodiment. A POSITA would have been motivated to make this combination at least because such embodiments are described in the same prior art reference, are fully compatible with each other,

could have been combined with minimal effort to achieve predictable results, and to minimize radiation leakage. EX1002, ¶132.

C. Claims 3, 5-7, 15, and 35-37

As explained above, Norman renders obvious claim 1. *See* §VII(B) (claim 1). As explained above, the additional limitations of these claims are disclosed by Norman. *See* §§VI(C)-(G), (R)-(T) (claims 3, 5-7, 15, and 35-37). Therefore, these claims are rendered obvious by Norman. EX1002, ¶¶124-131, 133-144, 169-174.

D. Claim 16

Norman discloses and renders this claim obvious. *See* §VI(H). EX1002, ¶¶145-150.

E. Claims 18, 20-22, and 29-33

As explained above, Norman renders obvious claim 16. *See* §VII(D) (claim 16). As explained above, the additional limitations of these claims are disclosed by Norman. *See* §§VI(I)-(Q) (claims 18, 20-22, and 29-33). Therefore, these claims are rendered obvious by Norman. EX1002, ¶¶145-168.

VIII. GROUND 5: CLAIMS 1, 3-12, 14-26, AND 28-38 ARE OBVIOUS OVER HASSFJELL-HOFF AND NORMAN

A. Hassfjell-Hoff

See §IV(A). EX1002, ¶¶44-49, 175.

B. Norman

See §VI(A). EX1002, ¶¶120-123, 176.

C. Motivation to Combine

1. Norman's gas-tight seal with Hassfjell-Hoff

To the extent that the gas-tight seal is construed as modifying the volume (See §III(D)(2) (second 1c construction)), a POSITA would have found it obvious to implement Hassfjell-Hoff such that there is a gas-tight seal around the collection container during collection as disclosed by Norman. Specifically, a POSITA would have been motivated to establish a gas-tight seal between the bottom end Hassfjell-Hoff's tube and the neck of the polyethylene bottle when the filtering basket is lowered into the interior of the polyethylene bottle. This is because a gas-tight seal between the bottom of the tube and the polyethylene bottle would limit the radioactive contamination on the outside of the polyethylene bottle, particularly the shoulder portion of the bottle connected to the neck. For example, the opening of the polyethylene bottle in Fig. 1 of Hassfjell-Hoff has an inner diameter of 31mm while the tube has a diameter of 36mm, which enables the chamfered bottom of the tube to have an interference fit inside the opening of the polyethylene bottle when the tube is fully lowered. EX1003, Fig. 1. A POSITA would have found it obvious to configure the surface at the top of the inner neck of the polyethylene bottle to mate with the chamfered end of the tube to enhance the integrity with a gas-tight seal between the end of the tube and the bottle. In addition, the bottle is made of polyethylene, which a POSITA would have understood would not allow the radon

gas to escape. EX1003, 6 (“gas-tight collection chamber”). A POSITA would have been motivated to configure the Hassfjell-Hoff system to form a gas-tight seal between the tube and the polyethylene bottle to enhance safety for the worker that is replacing the collection container, and would have had a reasonable expectation of success because such gas-tight seals are well-known. EX1002, ¶177.

Specifically, a POSITA would have been motivated to combine Hassfjell-Hoff and Norman to implement the Hassfjell-Hoff system with Norman’s gas tight seal on the collection chamber. *See* §§III(D)(1), (2) (construction of “fluidly coupled” and limitation 1c second construction). A POSITA would have understood that doing so would have been advantageous because the gas tight seal on the collection chamber of Norman would reduce the possibility of outside contamination or allowing radioactivity to escape the container. EX1007, 2:49-52 (“This invention is directed to a simple and inexpensive process and a generator for producing radioactive isotopes which is rapid, simple and substantially free of contamination.”). Norman discloses using a gas tight seal on the collection chamber. EX1007, 7:22-25 (“If the receiving chamber is also closed, i.e., both plungers 22 and 30 are inserted and secured with end caps 24 and 32, the escape of radon from the generator is prevented.”). A POSITA would have understood that there were well-known ways to create a gas-tight seal on the collection chamber, for example using sealed containers that are compatible with radiopharmaceuticals.

EX1017, Cover, Figs. 3-9. This modification would have been within the skill and knowledge of a POSITA, would have led to predictable results, would have created a reasonable expectation of success, would have been compatible with Hassfjell-Hoff, and would have been a mere design choice. EX1002, ¶178.

2. Norman's ceramic precursor isotope source with Hassfjell-Hoff

A POSITA would have been motivated to combine Hassfjell-Hoff and Norman to substitute the barium stearate precursor isotope source of Hassfjell-Hoff with the ceramic precursor isotope source of Norman because Norman lists barium stearate and inert ceramic as alternative materials acceptable for use with ^{228}Th as a precursor isotope source. EX1007, 3:44-56. Norman further identifies a porous matrix as an acceptable alternative to the inert ceramic material. EX1007, 7:48-59. These modifications would have been within the skill and knowledge of a POSITA, would have led to predictable results, would have created a reasonable expectation of success, would have been compatible with Hassfjell-Hoff, and would have been a mere design choice. EX1002, ¶179.

3. Norman's radiopharmaceutical with Hassfjell-Hoff

A POSITA would also have been motivated to combine Hassfjell-Hoff and Norman to implement the Hassfjell-Hoff system to form a radiopharmaceutical as disclosed in Norman. A POSITA would have understood that doing so would have been advantageous because ^{212}Pb was known to be a radioactive material useful as

a radioisotope and would have looked to Norman to describe how to formulate a radiopharmaceutical. EX1007, Abstract, 1:17-24. These modifications would have been within the skill and knowledge of a POSITA, would have led to predictable results, would have created a reasonable expectation of success, and would have been compatible with Hassfjell-Hoff. EX1002, ¶180.

D. Claim 1

Hassfjell-Hoff and Norman render this claim obvious. EX1002, ¶181.

1. **[1pre] “A radioisotope generator comprising:”**
[1a] “a solid precursor isotope source configured to emanate one or more gaseous progeny isotopes”
[1b] “the solid precursor isotope source comprising a precursor isotope; and
....
[1d] “wherein the solid precursor isotope source and the collector surface are configured such that the one or more gaseous progeny isotopes deposit one or more solid progeny isotopes on the collector surface.”

Hassfjell-Hoff discloses these limitations. *See* §§IV(B)(1)-(3), (5)

(limitations 1pre, 1a, 1b, 1d). EX1002, ¶182.

2. **[1c] “wherein the solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface with a gas tight seal, and”**

As explained above, this limitation is disclosed by Hassfjell-Hoff (§IV(B)(4) (limitation 1c)) and is disclosed by Norman (§VI(B)(4) (limitation 1c)). Moreover, this limitation is obvious by Hassfjell-Hoff in view of Norman. §III(D)(1), (2) (construction of “fluidly coupled” and limitation 1c constructions). To the extent

this claim is construed to require a gas-tight seal on the collection chamber during collection, a POSITA would have been motivated to modify Hassfjell-Hoff to include a gas-tight seal as taught by Norman. *See* §VIII(C)(1) (motivation to combine Norman's gas-tight seal with Hassfjell-Hoff). EX1002, ¶183-184.

E. Claims 3-4, 7-12, 14-15, 35-36, and 38

As explained above, Hassfjell-Hoff in view of Norman renders obvious claim 1. *See* §VIII(D) (claim 1). As explained above, the additional limitations of these claims are disclosed by Hassfjell-Hoff. *See* §§IV(C)-(L), (AA)-(CC) (claims 3-4, 7-12, 14-15, 35-36, and 38). Therefore, these claims are rendered obvious by Hassfjell-Hoff in view of Norman. EX1002, ¶¶181-186.

F. Claim 16

Hassfjell-Hoff in view of Norman renders this claim obvious. *See* §IV(M); §VI(H); §VIII(D). EX1002, ¶187.

G. Claims 17-19, 22-26, 28-29, 31-32, and 34

As explained above, Hassfjell-Hoff in view of Norman renders obvious claim 16. *See* §VIII(F) (claim 16). As explained above, the additional limitations of these claims are disclosed by Hassfjell-Hoff. *See* §§IV(N)-(Z) (claims 17-19, 22-26, 28-29, 31-32, and 34). Therefore, these claims are rendered obvious by Hassfjell-Hoff in view of Norman. EX1002, ¶¶187-189.

H. Claims 5-6, 20-21, 33, and 37

As explained above, these claims are disclosed and rendered obvious by Norman. *See* §§VI(D)-(E), (J)-(K), (Q), (T) (claims 5-6, 20-21, 33, and 37). Moreover, these limitations are obvious by Hassfjell-Hoff in view of Norman. *See* §§VIII(D), (F) (claims 1, 16). A POSITA would have been motivated by Norman to use a ceramic with the ^{228}Th precursor isotope in place of the solid precursor isotope source disclosed in Hassfjell-Hoff. *See* §VIII(C)(2) (motivation to combine). Further, a POSITA would have been motivated by Norman to use a porous material in place of the solid precursor isotope source disclosed in Hassfjell-Hoff. *See* §VIII(C)(2) (motivation to combine). A POSITA would have known that the precursor isotope would be encapsulated by the porous material. *See* §VIII(C)(2) (motivation to combine). EX1002, ¶¶181-184, 187, 190-191.

I. Claim 30 “The method of claim 16, further comprising forming a radiopharmaceutical using the one or more solid progeny isotopes.”

As explained above, this claim is disclosed and rendered obvious by Norman. *See* §VI(N) (claim 30); §VII(E) (claim 30). Moreover, claim 30 is obvious by Hassfjell-Hoff in view of Norman. *See* §VIII(F) (claim 16). A POSITA would have been motivated by Norman to use the method disclosed by Hassfjell-Hoff to form a radiopharmaceutical using the ^{212}Pb progeny isotope. *See* §VIII(C)(3) (motivation to combine). EX1002, ¶¶187, 192-193.

IX. GROUND 6: CLAIM 2 IS OBVIOUS OVER HASSEFJELL-HOFF AND IAEA

A. Hassfjell-Hoff

See §IV(A). EX1002, ¶¶44-49, 194.

B. IAEA

IAEA is a reference document published in 2013 and entitled “Radiotracer Generators for Industrial Applications.” EX1008. IAEA was part of the “IAEA Radiation Technology Series No. 5,” published in 2013. EX1008, 1 (cover page), 5 (copyright notice page). “IAEA Radiation Technology Series No. 5,” was assigned ISBN 978-92-0-135410-5 (EX1008, 5) and was received by the University of Michigan Library on July 11, 2013. EX1008, 6 (forward page). As such, IAEI was published and available to the public no later than July 11, 2013. EX1008, 6. IAEA was publicly accessible and indexed as a publication in public catalogs such as *e.g.*, the WorldCat index. EX1014. EX1002, ¶195.

A POSITA would have understood that publications of international consortiums are reliable sources for information and would have been capable of accessing them well before the alleged filing date of the 437 patent. Accordingly, IAEA qualifies as prior art under (AIA) 35 U.S.C. §102(a). EX1002, ¶¶196-197.

IAEA discloses principles for the development of and examples of radionuclide generators that produce radionuclides. EX1008, 12-39. Among these radionuclide generators, IAEA discloses:

The most common radionuclide generators are based on sorption of the mother radionuclide on a column support material with subsequent and selective elution of the daughter radionuclide from the column with some elution agent (Fig. 6) while the mother remains on the column support.

EX1008, 18. Figure 6 of IAEA is reproduced below:

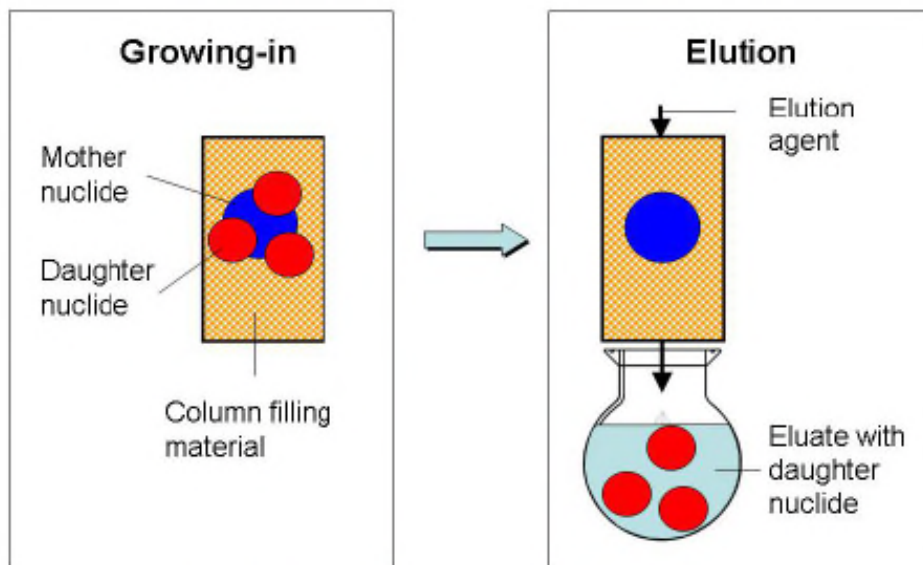


FIG. 6. Principle of a column based radionuclide generator.

EX1008, Fig. 6. As shown in Figure 6, an elution agent is added to the column to remove the daughter radionuclide for use. EX1002, ¶198.

Additional examples of radionuclide generators are shown in Figures 19 and 20 of IAEA:

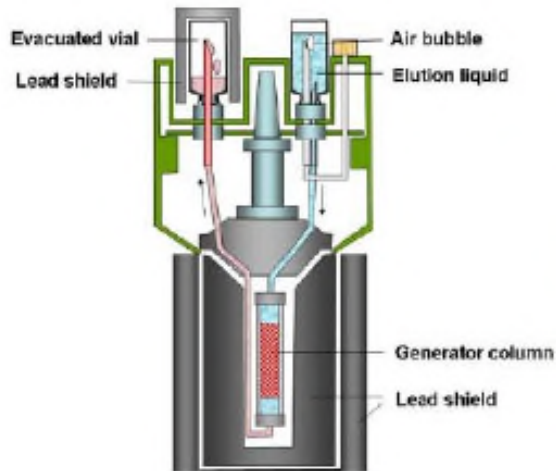


FIG 19. Left: A column generator in its lead shield. Elution is performed by a vacuum vial, also in a lead shield. Right: A typical lead-shielded and closed radionuclide generator.

EX1008, Fig. 19.

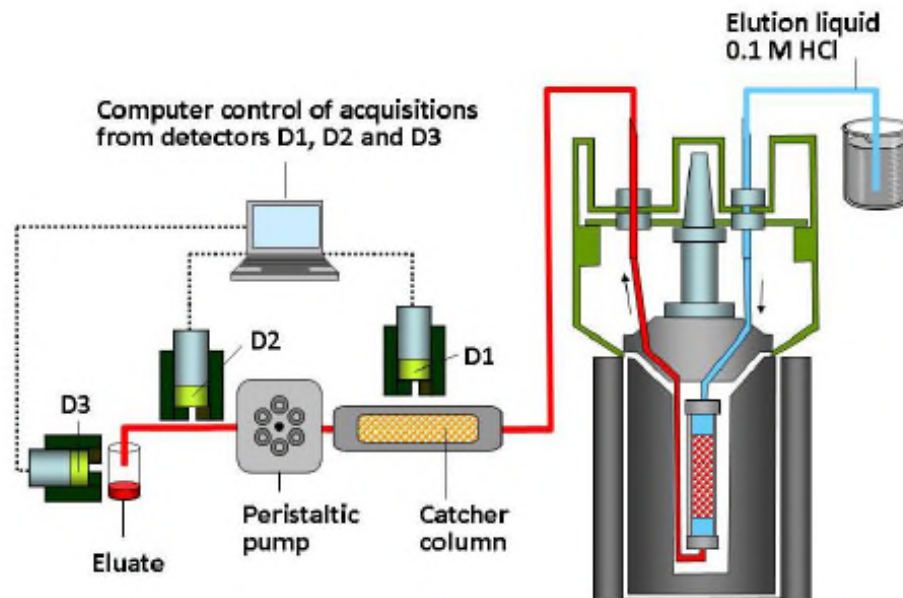


FIG 20. A generator set-up that is eluted by means of a peristaltic vacuum pump and with a catcher column outside the main generator housing for easy detection of mother radionuclide breakthrough.

EX1008, Fig. 20. EX1002, ¶199.

In each of Figures 19 and 20, a flushing circuit is shown that provides an elution liquid used to chelate the daughter radionuclide for removal from the system. EX1002, ¶200.

IAEA is analogous art to the 437 patent and was not considered during prosecution of the 437 patent. EX1001; EX1006. Moreover, as shown below, it was a material error for claim 2 of the 437 patent to issue over Hassfjell-Hoff in view of IAEA. EX1002, ¶¶201-202.

C. Claim 2 “The radioisotope generator of claim 1, further comprising a flushing circuit configured to flush the collector surface.”

Claim 2 is rendered obvious by Hassfjell-Hoff in view of IAEA. *See* §IV(B) (claim 1). EX1002, ¶203.

Hassfjell-Hoff discloses a radioisotope generator and a solvent used to flush the collector surface but does not explicitly disclose a flushing circuit configured to flush the collector surface. IAEA discloses such a flushing circuit. *See* §IX(B). IAEA discloses numerous examples of radionuclide generators that include an elution agent provided via a flushing circuit. EX1008, Figs. 6, 19, and 20. EX1002, ¶204.

A POSITA would have been motivated to modify Hassfjell-Hoff to include the flushing circuit of IAEA because including a flushing circuit in the Hassfjell-Hoff radioisotope generator would ease removal of the generated radioisotope

from the collector surface. Including a flushing circuit would have been within the skill and knowledge of a POSITA, would have led to predictable results, would have been compatible with Hassfjell-Hoff, and would have been a mere design choice. A POSITA would have had a reasonable expectation of success because IAEA teaches including a flushing circuit for use on radionuclide/radioisotope generators, and Hassfjell-Hoff teaches a radionuclide/radioisotope generator. Therefore, Hassfjell-Hoff in view of IAEA renders claim 2 obvious. EX1002, ¶205.

**X. GROUND 7: CLAIMS 13 AND 27 ARE OBVIOUS OVER
HASSFJELL-HOFF AND WESTRØM**

A. Hassfjell-Hoff

See §IV(A). EX1002, ¶¶44-49, 206.

B. Westrøm

Westrøm is a journal article published in 2017 and entitled “Preparation of ^{212}Pb -labeled monoclonal antibody using a novel ^{224}Ra -based generator solution.” EX1009, 1. Westrøm was included in volume 51 of the “Nuclear Medicine and Biology” Journal (EX1009, 1), which was published in August 2017. EX1009, 1 (cover page); EX1010. Volume 51 of the “Nuclear Medicine and Biology” Journal was assigned ISSN 0969-8051 (EX1009, 1) and was received by the National Library of Medicine on July 25, 2017. EX1009, 1 (cover page). As such, Westrøm

was published and available to the public no later than July 25, 2017. EX1009, 1. EX1002, ¶207.

Westrøm was publicly accessible and indexed as a publication in public catalogs such as e.g., the WorldCat index. EX1010. A POSITA would have understood that journals (e.g., EX1009) are reliable sources for information and would have been capable of accessing Westrøm well before the alleged filing date of the 437 patent. Accordingly, Westrøm qualifies as prior art under (AIA) 35 U.S.C. §102(a). EX1002, ¶¶208-209.

Westrøm discloses a method of producing ^{212}Pb -based radioimmunoconjugates from a ^{224}Ra -solution. See EX1009, 4. Westrøm discloses that in terms of ^{212}Pb -radiolabeling, the main improvement in protocol came with the emergence of the efficient lead-chelator TCMC (2-(4-isothiocyanatobenzyl)-1,4,7,10-tetraaza-1,4,7,10-tetra-(2-carbamoyl methyl)-cyclododecane). See EX1009, 5. Westrøm discloses “Many chelators have been assessed, including the commonly used p-SCN-Bn-DOTA (2-(4-isothiocyanatobenzyl)-1,4,7,10-tetraazacyclododecane tetraacetic acid), but TCMC has become the chelation chemistry of choice as it creates a more stable complex at lower pH and provides more efficient conjugation than its DOTA analog.” EX1009, 5. EX1002, ¶210.

Westrøm is analogous art to the 437 patent and was not considered during prosecution of the 437 patent. EX1001; EX1006. Moreover, as shown below, it

was material error for claims 13 and 27 of the 437 patent to issue over Hassfjell-Hoff in view of Westrøm. EX1002, ¶¶211-212.

C. Claim 13 “The radioisotope generator of claim 12, wherein the chelator comprises TCMC.”

Hassfjell-Hoff discloses and renders obvious claim 12. *See* §§IV(B), (F), (H), (J) (claims 1, 8, 10, 12); §§V(B)-(C) (claims 1, 8, 10, 12). Though Hassfjell-Hoff discloses use of a chelator, it does not expressly disclose “wherein the chelator comprises TCMC.” However, Westrøm, in the same field of endeavor, discloses a chelator that comprises TCMC. EX1009, 5. Indeed, Westrøm discloses that TCMC is preferable to DOTA, another commonly known chelating agent, as a chelating agent for ^{212}Pb . EX1009, 5 (“TCMC has become the chelation chemistry of choice as it creates a more stable complex at lower pH and provides more efficient conjugation than its DOTA analog.”). EX1002, ¶213.

A POSITA would have been motivated to use the TCMC chelator taught by Westrøm in the radioisotope generator of Hassfjell-Hoff because they are in the same field of radioisotope generation and would want to identify a chelating agent to recover ^{212}Pb efficiently. For that same reason, a POSITA would have had a reasonable expectation of success. Including TCMC as a chelator would have been within the skill and knowledge of a POSITA, would have led to predictable results, and would have been a mere design choice. Therefore, Hassfjell-Hoff in view of Westrøm renders claim 13 obvious. EX1002, ¶214.

D. Claim 27 “The method of claim 26, wherein the chelator comprises TCMC.”

Hassfjell-Hoff in view of Westrøm renders claim 27 obvious. *See* §VIII(C) (claim 13); §§IV(M), (R), (U) (claims 16, 23, 26); §§V(D)-(E) (claims 16, 23, 26). EX1002, ¶215.

XI. GROUND 8: CLAIMS 8-12, 14, 17, 23-26, 28, 34, AND 38 ARE OBVIOUS OVER NORMAN AND HASSFJELL-HOFF

A. Norman

See §VI(A). EX1002, ¶¶120-123, 216.

B. Hassfjell-Hoff

See §IV(A). EX1002, ¶¶44-49, 217.

C. Motivation to Combine

1. Hassfjell-Hoff’s container surface with Norman

A POSITA would have found it obvious to combine the teachings of Norman and Hassfjell-Hoff to modify Norman to collect ^{212}Pb on the interior container surface. Norman discloses collecting ^{212}Pb on an open porosity porous medium. Hassfjell-Hoff, which was published later and cites to Norman (EX1003, 6, 10), teaches collecting ^{212}Pb on an interior container surface. EX1002, ¶218.

A POSITA would have understood that any interior surface within a container could be a collector surface that collects the ^{212}Pb as the ^{220}Rn gas enters the container. A POSITA would have been motivated to collect ^{212}Pb in a container as disclosed by Hassfjell-Hoff because this is “a simpler and better approach.”

EX1003, 6. A POSITA would have been motivated to configure the Norman system to collect ^{212}Pb using a collector surface, including the structures disclosed by Hassfjell-Hoff. There would have been a reasonable expectation of success because both Hassfjell-Hoff and Norman disclose collecting ^{212}Pb from a collector surface. EX1003, 7; EX1007, 7:28-41. This modification would have been within the skill and knowledge of a POSITA, would have led to predictable results, would have created a reasonable expectation of success, would have been compatible with Norman, and would have been a mere design choice. EX1002, ¶219.

2. Hassfjell-Hoff's disposing a chelator on an interior surface with Norman

A POSITA would have found it obvious to modify Norman such that a chelator configured to chelate the one or more solid progeny isotopes is disposed on the interior surface of the container as disclosed by Hassfjell-Hoff. Specifically, a POSITA would have been motivated to dispose a chelator configured to chelate the one or more solid progeny isotopes on the interior surface as disclosed by Hassfjell-Hoff so that the amount of solid progeny isotopes recovered from the interior surface increases. EX1003, 7 (“About 70% of the radioactivity inside the polyethylene bottle can be easily washed off with approx. 30 ml of distilled water. By increasing the ionic strength of the washing solution or ***by adding a chelating agent, the yield increases.***”) (emphasis added). A POSITA would have been motivated to configure the Norman system based on the teachings of Hassfjell-

Hoff to increase the amount of ^{212}Pb recovered from the generator and would have had a reasonable expectation of success because both Norman and Hassfjell-Hoff disclose use of a chelator to recover ^{212}Pb . EX1003, 7; EX1007, Abstract, claim 9. This modification would have been within the skill and knowledge of a POSITA, would have led to predictable results, would have created a reasonable expectation of success, would have been compatible with Norman, and would have been a mere design choice. EX1002, ¶220.

3. Hassfjell-Hoff's use of a solvent in the container with Norman

A POSITA would have found it obvious to modify Norman so that the volume is configured to receive a solvent configured to dissolve the one or more solid progeny isotopes from the interior surface as disclosed by Hassfjell-Hoff. Specifically, a POSITA would have been motivated to receive a solvent in the volume as disclosed by Hassfjell-Hoff so that the amount of solid progeny isotopes recovered from the interior surface increases. EX1003, 7 (“About 70% of the radioactivity inside the polyethylene bottle can be easily washed off with approx. 30 ml of distilled water.”). A POSITA would have been motivated to configure the Norman system based on the teachings of Hassfjell-Hoff to increase the amount of ^{212}Pb recovered from the generator and would have had a reasonable expectation of success because both Norman and Hassfjell-Hoff disclose use of a solvent to recover ^{212}Pb . EX1003, 7; EX1007, 3:65-4:4. This modification would have been

within the skill and knowledge of a POSITA, would have led to predictable results, would have created a reasonable expectation of success, would have been compatible with Norman, and would have been a mere design choice. EX1002, ¶221.

4. Hassfjell-Hoff's flushing of the collector surface with Norman

A POSITA would have found it obvious to modify Norman to flush the collector surface as disclosed by Hassfjell-Hoff. Specifically, a POSITA would have been motivated to flush the collector surface so that the amount of solid progeny isotopes recovered from the interior surface increases. EX1003, 7 (“About 70% of the radioactivity inside the polyethylene bottle can be easily washed off with approx. 30 ml of distilled water.”). A POSITA would have been motivated to configure the Norman system based on the teachings of Hassfjell-Hoff to increase the amount of ^{212}Pb recovered from the generator and would have had a reasonable expectation of success because both Norman and Hassfjell-Hoff disclose using a recovering agent, such as water, to recover the solid progeny isotope. EX1003, 7; EX1007, 3:65-4:11. This modification would have been within the skill and knowledge of a POSITA, would have led to predictable results, would have created a reasonable expectation of success, would have been compatible with Norman, and would have been a mere design choice. EX1002, ¶222.

D. Claim 8 “The radioisotope generator of claim 1, wherein the collector surface is an interior surface of a container, and wherein the volume is an internal volume of the container.”

Norman discloses and renders obvious claim 1. *See* §VI(B) (claim 1); §VII(B) (claim 1). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(F) (claim 8). Moreover, this limitation is obvious by Norman in view of Hassfjell-Hoff. A POSITA would have been motivated to modify Norman to include a collector surface that is an interior surface of a container and a volume that is an internal volume of the container as taught by Hassfjell-Hoff. *See* §XI(C)(1) (motivation to combine). EX1002, ¶¶223-225.

E. Claim 9 “The radioisotope generator of claim 8, wherein the solid precursor isotope source is configured to be connected to an opening of the container.”

Norman in view of Hassfjell-Hoff renders obvious claim 8. *See* §XI(D) (claim 8). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §III(D)(3) (“connected to an opening of the container” construction). The container in Norman is analogous to the disclosed embodiments in the 437 patent, which are similarly containers with lids. *Compare* EX1007, Fig. 2, 7:65-8:12 (describing how the chamber is defined and includes a cap) *with* EX1001, Figs. 3A-3B, 14:25-36. Also, like the 437 patent, the solid precursor isotope source in Norman is affixed in the container using a

removable lid. *Compare* EX1007, Fig. 1 with EX1001, Fig. 5B. Thus, Norman's chambers 10 and 12 are connected with an opening to establish fluid communication between chambers 10 and 12, and the precursor isotope source in chamber 10 is located such that it connects it to the opening of chamber 12. EX1002, ¶¶226-228.

F. Claim 10 “The radioisotope generator of claim 8, further comprising the container.”

Norman in view of Hassfjell-Hoff renders obvious claim 8. *See* §XI(D) (claim 8). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Specifically, Norman discloses container 100. EX1007, Fig. 2. EX1002, ¶¶229-231.

G. Claim 11 “The radioisotope generator of claim 10, wherein the container is configured to removably connect to the solid precursor isotope source.”

Norman in view of Hassfjell-Hoff renders obvious claim 10. *See* §§XI(D), (F) (claims 8, 10). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §III(D)(4) (“removably connect” construction). Norman's solid precursor isotope source is affixed to a removable lid, such that the solid precursor isotope source is removably connected to the container. EX1007, Fig. 1, 6:9-47, 7:65-8:19. EX1002, ¶¶232-234.

H. Claim 12 “The radioisotope generator of claim 10, further comprising a chelator disposed on the interior surface, the chelator configured to chelate the one or more solid progeny isotopes.”

Norman in view of Hassfjell-Hoff renders obvious claim 10. *See* §§XI(D), (F) (claims 8, 10). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman discloses that the open porosity porous medium is contained within a receiving chamber. EX1007, 2:24-25 (“a receiving chamber containing an open porosity porous medium”). Norman discloses that the open porosity porous medium includes a lyophilized antibody conjugated to a chelator (*i.e.*, a chelating agent). *See* EX1007, claim 8 (“wherein said open porosity porous medium is lyophilized antibody.”), claim 9 (“wherein said lyophilized antibody is conjugated to a chelating agent.”). A POSITA would have understood that an open porosity porous medium disposed within a receiving chamber would contact the interior surface of the receiving chamber and that a chelating agent would chelate one or more solid progeny isotopes. EX1002, ¶¶235-237.

Alternatively, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(J) (claim 12). A POSITA would have been motivated to modify Norman to dispose a chelator on an interior surface of a container that is configured to chelate the one or more solid

progeny isotopes as taught by Hassfjell-Hoff. *See* §XI(C)(2) (motivation to combine). EX1002, ¶238.

I. Claim 14 “The radioisotope generator of claim 10, wherein the volume is configured to receive a solvent configured to dissolve the one or more solid progeny isotopes from the interior surface.”

Norman in view of Hassfjell-Hoff renders obvious claim 10. *See* §§XI(D), (F) (claims 8, 10). Norman discloses dissolving the open porosity porous medium with a solvent (*i.e.*, water). EX1007, 4:47 (“solvent, such as water”). Norman discloses that the solvent is *configured to dissolve the one or more solid progeny isotopes (i.e., ²¹²Pb) from the interior surface (i.e., the interior surface of the container)*. EX1007, Abstract (“diffusing the ²²⁰Rn gas into a second chamber, where it decays to ²¹²Pb which can then be collected from the second chamber.... The ²¹²Pb can be recovered from this medium by dissolving the medium.”), 3:65-4:4 (“As used herein, ‘recovering’ as it refers to the desired daughter isotopes means obtaining the daughter isotopes either with or from the open porosity porous medium. For example, where the open porosity porous medium is water soluble, the open porosity porous medium can be dissolved in water in order to obtain a solution whose principal radioactivity results from the daughter isotopes.”). EX1002, ¶¶239-241.

Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(K) (claim 14).

Specifically, Hassfjell-Hoff discloses that a volume is configured to receive a solvent. *See* §IV(K) (claim 14). A POSITA would have been motivated to modify the volume of Norman to be configured to receive a solvent as taught by Hassfjell-Hoff. *See* §XI(C)(3) (motivation to combine). EX1002, ¶242.

J. Claim 17 “The method of claim 16, further comprising flushing the collector surface.”

Norman discloses and renders obvious claim 16. *See* §VI(H) (claim 16); §VII(H) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(N) (claim 17). A POSITA would have been motivated to modify Norman to flush the collector surface as taught by Hassfjell-Hoff. *See* §XI(C)(4) (motivation to combine). EX1002, ¶¶243-245.

K. Claim 23 “The method of claim 16, wherein the collector surface is an interior surface of a container, and wherein the volume is an internal volume of the container.”

Norman discloses and renders obvious claim 16. *See* §VI(H) (claim 16); §VII(H) (claim 16). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(R) (claim 23), §XI(D) (claim 8). A POSITA would have been motivated to modify Norman to include a collector surface that is an interior surface of a container and a volume that is an internal volume of the container as taught by Hassfjell-Hoff. *See* §XI(D) (claim 8); §XI(C)(1) (motivation to combine). EX1002, ¶¶246-248.

L. Claim 24 “The method of claim 23, further comprising connecting the solid precursor isotope source to an opening of the container.”

Norman in view of Hassfjell-Hoff renders obvious claim 23. *See* §XI(K) (claim 23). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman discloses connecting the solid precursor isotope source to an opening of the container. *See* §§XI(E), (G) (claims 9, 11). EX1002, ¶¶249-251.

M. Claim 25 “The method of claim 23, further comprising removably connecting the solid precursor isotope to an opening of the container.”

Norman in view of Hassfjell-Hoff renders obvious claim 23. *See* §XI(K) (claim 23). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman discloses removably connecting a solid precursor isotope (^{228}Th is a solid disposed in the matrix) to an opening of the container. *See* §XI(G) (claim 11). EX1002, ¶¶252-254.

N. Claim 26 “The method of claim 23, further comprising chelating the one or more solid progeny isotopes using a chelator disposed on the interior surface.”

Norman in view of Hassfjell-Hoff renders obvious claim 23. *See* §XI(K) (claim 23). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §XI(H) (claim 12). A POSITA would have understood that an open porosity porous medium disposed within a receiving chamber would contact the interior surface of the receiving chamber and

that a chelating agent would chelate one or more solid progeny isotopes. EX1002, ¶¶255-257.

Alternatively, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed in an enabling manner. *See* §XI(H) (claim 12). A POSITA would have been motivated to modify Norman to dispose a chelator on an interior surface of a container that is configured to chelate the one or more solid progeny isotopes as taught by Hassfjell-Hoff. *See* §XI(H) (claim 12); §XI (C)(2) (motivation to combine). EX1002, ¶258.

O. Claim 28 “The method of claim 23, further comprising receiving a solvent in the volume, and dissolving the one or more solid progeny isotopes from the interior surface in the solvent.”

Norman in view of Hassfjell-Hoff renders obvious claim 23. *See* §XI(K) (claim 23). Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(V) (claim 28). A POSITA would have been motivated to modify Norman to receive a solvent in the volume and dissolve the one or more solid progeny isotopes from the interior surface in the solvent as taught by Hassfjell-Hoff. §XI(C)(3) (motivation to combine). EX1002, ¶¶259-261.

P. Claim 34 “The method of claim 23, forming at least a portion of a single chamber with the solid precursor isotope source and the container.”

This claim is indefinite. *See* §XIV(C). To the extent Patent Owner argues that this claim should be construed to require “[t]he method of claim 23, **further comprising,**” Norman in view of Hassfjell-Hoff renders obvious claim 23. *See* §XI(K) (claim 23). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman’s system includes a valve (*i.e.*, “stopcock”) that opens/closes, such that when it is opened there is a *single chamber* that includes *the solid precursor isotope source and the container*. EX1007, 8:30-41; §III(D)(6) (“with” construction). When the gate valve is closed there are two separate chambers. Thus, opening the gate valve *form[s]...a single chamber*. EX1002, ¶¶262-265.

Q. Claim 38 “The radioisotope generator of claim 10, wherein the solid precursor isotope source and the container form at least a portion of a single chamber when fluidly coupled.”

Norman in view of Hassfjell-Hoff renders obvious claim 10. *See* §XI(D), (F) (claims 8, 10). Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman’s *solid precursor isotope source and the container form at least a portion of a single chamber when fluidly coupled*. *See* §XI(P) (claim 34). EX1002, ¶¶266-268.

XII. GROUND 9: CLAIMS 13 AND 27 ARE OBVIOUS OVER NORMAN, HASSFJELL-HOFF, AND WESTRØM

A. Norman

See §VI(A). EX1002, ¶¶120-123, 269.

B. Hassfjell-Hoff

See §IV(A). EX1002, ¶¶44-49, 270.

C. Westrøm

See §X(B). EX1002, ¶¶207-212, 271.

D. Claim 13 “The radioisotope generator of claim 12, wherein the chelator comprises TCMC.”

Norman in view of Hassfjell-Hoff renders obvious claim 12. *See* §XI(H) (claim 12). Though Norman and Hassfjell-Hoff each disclose the use of a chelator, neither Norman nor Hassfjell-Hoff expressly discloses “wherein the chelator comprises TCMC.” However, Westrøm, in the same field of endeavor, discloses a chelator that comprises TCMC. EX1009, 5. Indeed, Westrøm discloses that TCMC is preferable to DOTA, another commonly known chelating agent, as a chelating agent for ²¹²Pb. EX1009, 5 (“TCMC has become the chelation chemistry of choice as it creates a more stable complex at lower pH and provides more efficient conjugation than its DOTA analog.”). EX1002, ¶¶272-274.

A POSITA would have been motivated to use the TCMC chelator taught by Westrøm in the radioisotope generator of Norman in view of Hassfjell-Hoff because they are in the same field of radioisotope generation and would want to

identify a chelating agent to recover ^{212}Pb efficiently. For that same reason, a POSITA would have had a reasonable expectation of success. Including TCMC as a chelator would have been within the skill and knowledge of a POSITA, would have led to predictable results, and would have been a mere design choice. Therefore, Norman in view of Westrøm renders claim 13 obvious. EX1002, ¶275.

E. Claim 27 “The method of claim 26, wherein the chelator comprises TCMC.”

Norman in view of Hassfjell-Hoff renders obvious claim 26. *See* §XI(N) (claim 26). Westrøm further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Westrøm discloses the use of TCMC as a chelator. *See* §XII(D) (claim 13). EX1002, ¶¶276-278.

XIII. GROUND 10: CLAIMS 13 AND 27 ARE OBVIOUS OVER HASSFJELL-HOFF, NORMAN AND WESTRØM

A. Hassfjell-Hoff

See §IV(A). EX1002, ¶¶44-49, 279.

B. Norman

See §VI(A). EX1002, ¶¶120-123, 280.

C. Westrøm

See §X(B). EX1002, ¶¶207-212, 281.

D. Claim 13 “The radioisotope generator of claim 12, wherein the chelator comprises TCMC.”

Hassfjell-Hoff in view of Norman discloses and renders obvious claim 12. *See* §VIII(E) (claim 12). Though Hassfjell-Hoff and Norman each disclose the use of a chelator, neither Hassfjell-Hoff nor Norman expressly discloses “wherein the chelator comprises TCMC.” However, Westrøm, in the same field of endeavor, discloses a chelator that comprises TCMC. EX1009, 5. Indeed, Westrøm discloses that TCMC is preferable to DOTA, another commonly known chelating agent, as a chelating agent for ^{212}Pb . EX1009, 5 (“TCMC has become the chelation chemistry of choice as it creates a more stable complex at lower pH and provides more efficient conjugation than its DOTA analog.”). EX1002, ¶¶282-284.

A POSITA would have been motivated to use the TCMC chelator taught by Westrøm in the radioisotope generator of Hassfjell-Hoff as modified by Norman because Hassfjell-Hoff, Norman, and Westrøm are in the same field of radioisotope generation and a POSITA would want to identify a chelating agent to recover ^{212}Pb efficiently. For that same reason, a POSITA would have had a reasonable expectation of success. Including TCMC as a chelator would have been within the skill and knowledge of a POSITA, would have led to predictable results, and would have been a mere design choice. Therefore, Hassfjell-Hoff in view of Norman and Westrøm renders claim 13 obvious. EX1002, ¶285.

E. Claim 27 “The method of claim 26, wherein the chelator comprises TCMC.”

Hassfjell-Hoff in view of Norman renders obvious claim 26. *See* §VII(H) (claim 26). Westrøm further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Westrøm discloses the use of TCMC as a chelator. *See* §XIII(D) (claim 13). EX1002, ¶¶286-288.

XIV. GROUND 11: CLAIMS 1-15 AND 34-38 ARE UNPATENTABLE UNDER 35 U.S.C. §112

A. Claims 1-15 and 35-38 are indefinite

As explained in Section III(D)(2), “wherein the solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface with a gas tight seal” has three equally possible meanings of it in the claims:

- The entire volume has a gas tight seal (with the precursor isotope source inside the volume),
- Just the collector surface, not the entire volume, has a gas tight seal (when the precursor isotope source is inside the collector), or
- The system is configured to selectively couple, using a gas tight seal, a volume with the solid precursor isotope source and a volume with a collector surface.

As a POSITA reading the 437 patent would be unable to determine the scope of the claims with reasonable certainty, the claims are indefinite. EX1002, ¶289.

Because independent claim 1 is indefinite, dependent claims 2-15 and 35-38 are indefinite. EX1002, ¶290.

B. Claim 10 fails to further limit claim 8

Claim 10 recites “The radioisotope generator of claim 8, further comprising the container.” However, claim 8 already includes a container. As claim 8 fails to add limitations to claim 8, it is invalid under the requirement in Section 112(d) that the claim “specify a further limitation of the subject matter claimed.”

C. The language of Claim 34 is non-sensical, therefore indefinite

Claim 34 recites “The method of claim 23, forming at least a portion of a single chamber with the solid precursor isotope source and the container.” Claim 34 lacks a transition phrase, such as “further comprising” or “further consisting of,” or an indication that claim 34 limits a method step of a parent claim.

Moreover, it is unclear what constitutes the “single chamber” and how the “single chamber” forms part of the generator. Accordingly, a POSITA is not able to determine the intended scope of claim 34. EX1002, ¶291.

XV. DISCRETIONARY DENIAL IS NOT WARRANTED

Pursuant to Acting Director Coke M. Stewart’s March 26, 2025, Memorandum regarding Interim Processes for PTAB Workload Management, Petitioner understands that discretionary denial issues, if any, will be raised in a separate brief to be filed by Patent Owner. If Patent Owner files such a brief, Petitioner intends to respond in an opposition brief consistent with Acting Director

Coke M. Stewart's March 26, 2025, Memorandum regarding Interim Processes for PTAB Workload Management.

In an effort to save the parties from unnecessary briefing on discretionary denial (though reserving the right to respond in the event that Patent Owner submits a brief requesting discretionary denial), Petitioner expressly addresses the clear material error by the Examiner. While Hassfjell-Hoff and Norman both appeared in an information disclosure statement (IDS) (EX1006, 145), the second prong of the *Advanced Bionics* framework strongly favors institution because the examiner erred in a manner material to the patentability of challenged claims. *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (P.T.A.B. Feb. 13, 2020) (precedential). In this case, the Hassfjell-Hoff and Norman prior art were never substantively evaluated during examination. In fact, there is no indication of any substantive evaluation of any prior art during examination because the Examiner allowed the application without issuing a single office action. EX1006. Moreover, Hassfjell-Hoff and Norman were not introduced to the Examiner prior to issuing the initial Notice of Allowance. EX1006. The Examiner's initial Notice of Allowance stated that the prior art in general does not provide adequate detail to address "exposing the collector surface to gaseous progeny isotopes to deposit solid progeny isotopes." EX1006, 239. However, Norman discloses this limitation as shown in VI(B)(5) above. EX1007,

Abstract, 2:65-3:11. Hassfjell-Hoff also discloses this limitation as shown in IV(B)(5) above. EX1003, 7. It was only after receiving the initial Notice of Allowance that Applicant then filed an RCE with an IDS citing Hassfjell-Hoff and Norman amongst numerous other references. EX1006, 276. In return, the Examiner quickly issued a second Notice of Allowance listing the same reasons for allowance as were set out in the initial Notice of Allowance and never mentioning Hassfjell-Hoff and Norman, nor any other cited art. EX1006, 379. This is clear material error because as shown above in Sections IV-XIII, the claims are invalid. The Board has declined to discretionarily deny institution where, as here, the prior art in question was not the subject of Examiner or applicant discussion or evaluation. *E.g., Satco Products Inc. v. The Regents of the Univ. of California*, IPR2021-00662, Paper 13 at 25 (P.T.A.B. Nov. 8, 2021). The Examiner's error in overlooking the asserted prior art is clear. See Sections IV-XIII.

XVI. MANDATORY NOTICES UNDER 37 C.F.R. §§ 42.8(B)(1)-(4)

A. Real Party-In-Interest

AdvanCell Pty Ltd. is the real party-in-interest.

B. Related Matters

The 437 patent is not subject to any related matters.

PGR2025-00029 is a petition for post grant review that was filed against a related patent—U.S. Patent No. 12,125,603—on March 10, 2025.

C. Lead and Backup Counsel

Lead Counsel	Backup Counsel
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D. Service Information

Service information for lead and backup counsel is provided in the designation of lead and backup counsel above. Petitioner consents to electronic service to lead and back-up counsel and to:

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XVII. CONCLUSION

All Challenged Claims of the 437 patent should be found unpatentable for the reasons discussed in this Petition.

Date: April 8, 2025

Respectfully submitted,

/s/ Jennifer Librach Nall

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CERTIFICATE OF WORD COUNT

Pursuant to 37 C.F.R. § 42.24(d), Petitioner certifies that this petition includes 17,812 words, as measured by Microsoft Word, exclusive of the table of contents, mandatory notices under § 42.8, certificates of service, word count, claim listing, and exhibits.

Date: April 8, 2025

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CERTIFICATE OF SERVICE

The undersigned certifies pursuant to 37 C.F.R. §§ 42.6(e) and 42.105 that on April 8, 2025, a true and correct copy of the Petition for post-grant review of U.S. Patent No. 12,249,437 was served via express mail on the Patent Owner at the below correspondence address of record:

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Respectfully submitted,

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