

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

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

I hereby declare under penalty of perjury under the laws of the United States of America that the following is true and correct, and that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true. I understand that willful false statements are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code.

4/8/2025 | 10:52 PDT

Date

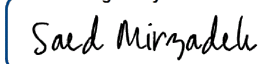
DocuSigned by:

00F538B3EA8E4BA...
Saed Mirzadeh

TABLE OF CONTENTS

	Page
I. BACKGROUND AND QUALIFICATION	2
A. Materials Considered.....	2
II. LEGAL STANDARDS	3
A. Legal Standards for Anticipation	3
B. Legal Standards for Obviousness.....	3
III. THE 437 PATENT	8
A. Overview of the 437 patent	8
B. Overview of the 437 patent’s File History	9
C. Person of Ordinary Skill in the Art	10
D. Claim Construction.....	11
1. “fluidly coupled” (claims 1, 16, 18, 29, and 38).....	11
2. Limitation 1c construction - “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)	11
3. “a valve associated with the solid precursor isotope source” (claim 3).....	15
4. “connected to an opening of the container” (claim 9)	15
5. “removably connect” (claim 11).....	15
6. “with” (claim 34)	15
IV. GROUND 1: CLAIMS 1, 3-4, 7-12, 14-19, 22-26, 28-29, 31-32, 34-36, AND 38 ARE ANTICIPATED AND RENDERED OBVIOUS BY HASSFJELL-HOFF	16
A. Hassfjell-Hoff.....	16
B. Claim 1	21
1. [1pre] “A radioisotope generator comprising:”	21
2. [1a] “a solid precursor isotope source configured to emanate one or more gaseous progeny isotopes”	23

3.	[1b] “the solid precursor isotope source comprising a precursor isotope; and”	24
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”	25
a.	First Construction	25
b.	Third Construction.....	27
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.”	28
C.	Claim 3 “The radioisotope generator of claim 1, further comprising a valve associated with the solid precursor isotope source.”	29
D.	Claim 4 “The radioisotope generator of claim 1, further comprising a vacuum pump attached to the volume.”	30
E.	Claim 7 “The radioisotope generator of claim 1, wherein the precursor isotope comprises a thorium 228 isotope (228Th) and/or a radium 224 isotope (224Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (220Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (212Pb).”	31
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.”	32
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.”	33
H.	Claim 10 “The radioisotope generator of claim 8, further comprising the container.”	35
I.	Claim 11 “The radioisotope generator of claim 10, wherein the container is configured to removably connect to the solid precursor isotope source.”	36

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.”	37
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.”	37
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.”	39
M.	Claim 16	40
2.	[16pre] “A method of generating a progeny radioisotope, the method comprising:”	40
3.	[16a] “allowing one or more gaseous progeny isotopes to emanate from a solid precursor isotope source”	40
4.	[16b] “the solid precursor isotope source comprising a precursor isotope”	41
5.	[16c] “fluidly coupling a volume including a collector surface to the solid precursor isotope source using a gas tight seal; and”	41
6.	[16d] “allowing one or more solid progeny isotopes of the one or more gaseous progeny isotopes to deposit on the collector surface.”	42
N.	Claim 17 “The method of claim 16, further comprising flushing the collector surface.”	42
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.”	43
P.	Claim 19 “The method of claim 16, further comprising drawing a vacuum in the volume.”	43

Q.	Claim 22 “The method of claim 16, wherein the precursor isotope comprises a thorium 228 isotope (228Th) and/or a radium 224 isotope (224Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (220Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (212Pb).”	44
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.”	44
S.	Claim 24 “The method of claim 23, further comprising connecting the solid precursor isotope source to an opening of the container.”	45
T.	Claim 25 “The method of claim 23, further comprising removably connecting the solid precursor isotope to an opening of the container.”	45
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.”	46
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.”	46
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.”	47
X.	Claim 31 “The method of claim 18, further comprising closing the valve to isolate the volume from the solid precursor isotope source.”	47
Y.	Claim 32 “The method of claim 16, wherein the solid precursor isotope is bound to a non-radioactive material.”	48

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.”	49
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.”	50
BB.	Claim 36 “The radioisotope generator of claim 1, wherein the solid precursor isotope is bound to a non-radioactive material.”	50
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.”	51
V.	GROUND 2: CLAIMS 1, 3, 5-7, 15-16, 18, 20-22, 29-33, AND 35-37 ARE ANTICIPATED AND RENDERED OBVIOUS BY NORMAN	51
A.	Norman	51
B.	Claim 1	54
1.	[1pre] “A radioisotope generator comprising:”	54
2.	[1a] “a solid precursor isotope source configured to emanate one or more gaseous progeny isotopes”	55
3.	[1b] “the solid precursor isotope source comprising a precursor isotope; and”	56
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”	56
a.	First and Second Constructions	56
a.	Third Construction	59
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.”	60
C.	Claim 3 “The radioisotope generator of claim 1, further comprising a valve associated with the solid precursor isotope source.”	61

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.”	61
E.	Claim 6 “The radioisotope generator of claim 5, wherein the precursor isotope is absorbed, adsorbed, and/or encapsulated by the porous material.”	62
F.	Claim 7 “The radioisotope generator of claim 1, wherein the precursor isotope comprises a thorium 228 isotope (228Th) and/or a radium 224 isotope (224Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (220Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (212Pb).”	63
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.”	63
H.	Claim 16	64
1.	[16pre] “A method of generating a progeny radioisotope, the method comprising:”	64
2.	[16a] “allowing one or more gaseous progeny isotopes to emanate from a solid precursor isotope source”	65
3.	[16b] “the solid precursor isotope source comprising a precursor isotope”	65
4.	[16c] “fluidly coupling a volume including a collector surface to the solid precursor isotope source using a gas tight seal; and”	65
5.	[16d] “allowing one or more solid progeny isotopes of the one or more gaseous progeny isotopes to deposit on the collector surface.”	65
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.”	65

J.	Claim 20 “The method of claim 16, wherein the solid precursor isotope source comprises a porous material configured to retain the precursor isotope.”	66
K.	Claim 21 “The method of claim 20, wherein the precursor isotope is absorbed, adsorbed, and/or encapsulated by the porous material.”	66
L.	Claim 22 “The method of claim 16, wherein the precursor isotope comprises a thorium 228 isotope (228Th) and/or a radium 224 isotope (224Ra), the one or more gaseous progeny isotopes comprises a radon 220 isotope (220Rn), and the one or more solid progeny isotopes comprises a lead 212 isotope (212Pb).”	67
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.”	67
N.	Claim 30 “The method of claim 16, further comprising forming a radiopharmaceutical using the one or more solid progeny isotopes.”	67
O.	Claim 31 “The method of claim 18, further comprising closing the valve to isolate the volume from the solid precursor isotope source.”	68
P.	Claim 32 “The method of claim 16, wherein the solid precursor isotope is bound to a non-radioactive material.”	69
Q.	Claim 33 “The method of claim 32, wherein the non-radioactive material is a ceramic.”	69
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.”	69
S.	Claim 36 “The radioisotope generator of claim 1, wherein the solid precursor isotope is bound to a non-radioactive material.”	70
T.	Claim 37 “The radioisotope generator of claim 36, wherein the non-radioactive material is a ceramic.”	70

VI.	GROUND 3: CLAIMS 1, 3-12, 14-26, AND 28-38 ARE OBVIOUS OVER HASSFJELL-HOFF AND NORMAN.....	70
A.	Hassfjell-Hoff.....	70
B.	Norman.....	71
C.	Motivation to Combine	71
D.	Claim 1	74
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.”	74
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”.....	74
E.	Claims 3-4, 7-12, 14-15, 35-36, and 38	75
F.	Claim 16	75
G.	Claims 17-19, 22-26, 28-29, 31-32, and 34	75
H.	Claims 5-6, 20-21, 33, and 37	76
I.	Claim 30 “The method of claim 16, further comprising forming a radiopharmaceutical using the one or more solid progeny isotopes.”	76
VII.	GROUND 4: CLAIM 2 IS OBVIOUS OVER HASSFJELL-HOFF AND IAEA	77
A.	Hassfjell-Hoff.....	77
B.	IAEA.....	77
C.	Claim 2 “The radioisotope generator of claim 1, further comprising a flushing circuit configured to flush the collector surface.”	80
VIII.	GROUND 5: CLAIMS 13 AND 27 ARE OBVIOUS OVER HASSFJELL-HOFF AND WESTRØM.....	82

A.	Hassfjell-Hoff.....	82
B.	Westrøm	82
C.	Claim 13 “The radioisotope generator of claim 12, wherein the chelator comprises TCMC.”	84
D.	Claim 27 “The method of claim 26, wherein the chelator comprises TCMC.”	85
IX.	GROUND 6: CLAIMS 8-12, 14, 17, 23-26, 28, 34, AND 38 ARE OBVIOUS OVER NORMAN AND HASSFJELL-HOFF	85
A.	Norman	85
B.	Hassfjell-Hoff.....	85
C.	Motivation to Combine	85
1.	Hassfjell-Hoff’s container surface with Norman.....	85
2.	Hassfjell-Hoff’s disposing a chelator on an interior surface with Norman.....	86
3.	Hassfjell-Hoff’s use of a solvent in the container with Norman.....	87
4.	Hassfjell-Hoff’s flushing of the collector surface with Norman.....	88
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.”	89
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.”	90
F.	Claim 10 “The radioisotope generator of claim 8, further comprising the container.”	91
G.	Claim 11 “The radioisotope generator of claim 10, wherein the container is configured to removably connect to the solid precursor isotope source.”	91
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.”	92

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.”	93
J.	Claim 17 “The method of claim 16, further comprising flushing the collector surface.”	94
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.”	95
L.	Claim 24 “The method of claim 23, further comprising connecting the solid precursor isotope source to an opening of the container.”	95
M.	Claim 25 “The method of claim 23, further comprising removably connecting the solid precursor isotope to an opening of the container.”	96
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.”	96
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.”	97
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.”	98
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.”	99
X.	GROUND 7: CLAIMS 13 AND 27 ARE OBVIOUS OVER NORMAN, HASSFJELL-HOFF, AND WESTRØM.....	99
A.	Norman	99
B.	Hassfjell-Hoff.....	99
C.	Westrøm	99
D.	Claim 13 “The radioisotope generator of claim 12, wherein the chelator comprises TCMC.”	100

E.	Claim 27 “The method of claim 26, wherein the chelator comprises TCMC.”.....	101
XI.	GROUND 8: CLAIMS 13 AND 27 ARE OBVIOUS OVER HASSFJELL-HOFF, NORMAN AND WESTRØM.....	101
A.	Hassfjell-Hoff.....	101
B.	Norman	101
C.	Westrøm	102
D.	Claim 13 “The radioisotope generator of claim 12, wherein the chelator comprises TCMC.”.....	102
E.	Claim 27 “The method of claim 26, wherein the chelator comprises TCMC.”.....	103
XII.	GROUND 9: CLAIMS 1-15 AND 34-38 ARE UNPATENTABLE UNDER 35 U.S.C. §112.....	103
A.	Claims 1-15 and 35-38 are indefinite.....	103
B.	The language of Claim 34 is non-sensical, therefore indefinite	104
XIII.	SECONDARY CONSIDERATIONS	105
XIV.	AVAILABILITY FOR CROSS-EXAMINATION	105
XV.	RIGHT TO SUPPLEMENT	105
XVI.	CONCLUSION.....	106

INDEX OF EXHIBITS

Exhibit No.	Description
1001	U.S. Patent No. 12,249,437.
1002	RESERVED
1003	Hassfjell, Sindre P. and Hoff, Per, “A Generator for Production of ^{212}Pb and ^{212}Bi ”, Appl. Radiat. Isot., vol. 45, no. 10, pp 6-25 (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 .
1017	U.S. Patent No. 9,281,089.
1018	U.S. Patent No. 6,932,111 (“ Ishigaki ”).

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, Saed Mirzadeh, declare as follows:

1. My name is Saed Mirzadeh. I have been asked by Petitioner AdvanCell Pty Ltd. (“Petitioner”) to provide my expert opinions in support of the above-identified petition for *post grant* review of claims 1-38 (“Challenged Claims”) of U.S. Patent No. 12,249,437 (“437 patent,” EX1001). I have been informed that the 437 patent is owned by Sciencons AS (“Sciencons AS”).

2. I currently hold the opinions set forth in this Declaration.

3. In summary, it is my opinion that the references cited below render unpatentable the Challenged Claims. My detailed opinions on the claims are set forth below. In this Declaration, I offer opinions on 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	102/103	Hassfjell-Hoff
2	1, 3, 5-7, 15-16, 18, 20-22, 29-33, 35-37	102/103	Norman
3	1, 3-12, 14-26, 28-38	103	Hassfjell-Hoff and Norman
4	2	103	Hassfjell-Hoff and IAEA
5	13, 27	103	Hassfjell-Hoff and Westrøm
6	8-12, 14, 17, 23-26, 28, 34, 38	103	Norman and Hassfjell-Hoff

Ground	Claims	Stat. Basis	Prior Art
7	13, 27	103	Norman, Hassfjell-Hoff, and Westrøm
8	13, 27	103	Hassfjell-Hoff, Norman, and Westrøm
9	1-15, 34-38	112	

4. I am being compensated for my time at the rate of \$300 per hour. This compensation is not contingent upon my performance, the outcome of this matter, or any issues involved in or related to this matter.

I. BACKGROUND AND QUALIFICATION

5. All of my opinions stated herein are based on my own personal knowledge, professional judgment, and analysis of the materials and information I considered in preparing this Declaration. In forming my opinions, I have relied on my knowledge and experience in designing, developing, researching, and teaching the technology referenced in this Declaration.

6. I am over 18 years of age and, if I am called upon to do so, I would be competent to testify as to the matters set forth herein. I understand that a copy of my current curriculum vitae, which details my education and professional and academic experience, is being submitted as Appendix 1.

A. Materials Considered

7. In preparing this Declaration, I have reviewed and/or considered at least the documents cited in the Index of Exhibits, and the documents referenced in this Declaration. I have also reviewed the prosecution history of the 437 patent.

II. LEGAL STANDARDS

A. Legal Standards for Anticipation

8. I have been informed that documents and materials that qualify as prior art can be used to invalidate a patent claim via anticipation or obviousness.

9. I have been informed that, once the claims of a patent have been properly construed, the second step in determining anticipation of a patent claim requires a comparison of the properly construed claim language to the prior art on a limitation-by-limitation basis.

10. I have been informed that a prior art reference “anticipates” an asserted claim, and thus renders the claim invalid, if all elements of the claim are disclosed in that prior art reference, either explicitly or inherently (*i.e.*, necessarily present), arranged as claimed and in an enabling manner.

11. I have been informed that anticipation in a post grant review must be shown by a preponderance of the evidence.

B. Legal Standards for Obviousness

12. I have been informed that even if a patent claim is not anticipated, it is still invalid if the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the pertinent art.

13. I have been informed that a person of ordinary skill in the art provides a reference point from which the prior art and claimed invention should be viewed.

This reference point prevents one from using his or her own insight or hindsight in deciding whether a claim is obvious.

14. I also have been informed that an obviousness determination includes the consideration of various factors such as (1) the scope and content of the prior art, (2) the differences between the prior art and the asserted claims, (3) the level of ordinary skill in the pertinent art, and (4) the existence of secondary considerations such as commercial success, long-felt but unresolved needs, failure of others, etc.

15. I have been informed that an obviousness evaluation can be based on a combination of multiple prior art references. I have been informed that the prior art references themselves may provide a suggestion, motivation, or reason to combine, but other times the nexus linking two or more prior art references is simple common sense. I further have been informed that obviousness analysis recognizes that market demand, rather than scientific literature, often drives innovation, and that a motivation to combine references may be supplied by the direction of the marketplace.

16. I have been informed that if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.

17. I have been informed that practical and common-sense considerations should guide a proper obviousness analysis, because familiar items may have obvious uses beyond their primary purposes. I have been informed that a person of ordinary skill in the art looking to overcome a problem will often be able to fit together the teachings of multiple publications. I have been informed that an obviousness analysis therefore takes into account the inferences and creative steps that a person of ordinary skill in the art would employ under the circumstances.

18. I have been informed that a particular combination may be proven obvious merely by showing that it was obvious to try the combination. For example, when there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp because the result is likely the product not of innovation but of ordinary skill and common sense.

19. I have been informed that the combination of familiar elements according to known methods is likely to be obvious when it does no more than have predictable results. I have been informed that when a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. I have also been informed that if a

person of ordinary skill can implement a predictable variation, the patent claim is likely obvious.

20. I have been informed that a proper obviousness analysis focuses on what was known or obvious to a person of ordinary skill in the art, not just the patentee. Accordingly, I have been informed that any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.

21. I have been informed that a proposed obviousness combination does not need to be the preferred, or most desirable, combination available, in order to render a claim obvious. I have been informed that, instead, there must be something that suggests the desirability of the proposed combination, not necessarily something that suggests that the proposed combination is the most desirable combination available.

22. Similarly, I have been informed that for purposes of obviousness, when a motivating benefit comes at the expense of another benefit, that does not nullify the proposed obviousness combination or modification. Likewise, I have been informed that a proposed obviousness combination does not fail merely because it may be inferior to other systems used for the same use.

23. I have been informed that a determination of obviousness based on teachings from multiple references does not require an actual, physical substitution

of elements between the multiple references. I have been informed that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference. Instead, I have been informed that the test is whether a claim is rendered obvious by the teachings of the prior art as a whole.

24. I have been informed that a claim can be obvious in light of a single reference, without the need to combine references, if the elements of the claim that are not found explicitly or inherently in the reference can be supplied by the common sense of one of skill in the art.

25. I have been informed that secondary indicia of non-obviousness may include: (1) a long felt but unmet need in the prior art that was satisfied by the invention of the patent; (2) commercial success of processes covered by the patent; (3) unexpected results achieved by the invention; (4) praise of the invention by others skilled in the art; (5) taking of licenses under the patent by others; (6) deliberate copying of the invention; (7) failure of others to find a solution to the long felt need; and (8) skepticism by experts.

26. I have been informed that there must be a relationship between any such secondary considerations and the invention. I have been informed that contemporaneous and independent invention by others is a secondary consideration supporting an obviousness determination.

27. In sum, my understanding is that prior art teachings are properly combined where a person of ordinary skill in the art having the understanding and knowledge reflected in the prior art and motivated by the general problem facing the inventor, would have been led to make the combination of elements recited in the claims. Under this analysis, the prior art references themselves, or any need or problem known in the field of endeavor at the time of the invention, can provide a reason for combining the elements of multiple prior art references in the claimed manner.

28. I have been informed that obviousness in a post grant review must be shown by a preponderance of the evidence.

III. THE 437 PATENT

A. Overview of the 437 patent

29. 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.

30. I have been informed that, based on the face of the patent, the priority date for this patent is December 5, 2019.

B. Overview of the 437 patent's File History

31. The 437 patent was filed on May 31, 2024 as a continuation application of U.S. Patent Application No. 17/756,802 (now U.S. Patent No. 12,125,603). EX1001, cover. EX1006, 356. The continuation application was filed with claims 1-30. EX1006, 395-399. The continuation application was filed with a Track One request. EX1006, 369. The 437 patent was first published on November 28, 2024 as U.S. Patent Application Publication No. 2024/0395432. EX1001, Cover. EX1006, 103. The Track One request was granted on August 6, 2024. EX1006, 244. The examiner never issued a rejection based on the prior art that I describe in this Declaration or on any other prior art, and sent a first Notice of Allowability on September 25, 2024. EX1006, 166. A Preliminary Amendment, an Information Disclosure Statement, and a Request for Continued Examination were filed on November 13, 2024 amending claim 11 and adding claims 31-38. EX1006, 144-153. A Second Notice of Allowability was sent by the USPTO on December 5, 2024. EX1006, 26. As stated in both the Notice of Allowability and the Second Notice of Allowability, the Examiner's reasons for allowance were:

The prior art in general discloses the decay of solid precursor isotopes in a collection container in general, but does not provide adequate detail to address the inventive features of exposing the collector surface to gaseous progeny isotopes to deposit solid

progeny isotopes. The information provided in the prior art does not address these features, or provide a basis for a person of ordinary skill in the art to arrive at them without relying on improper hindsight reasoning or inappropriate claim interpretation.

EX1006, 31, 171.

32. On January 27, 2025, the Applicant filed an amendment after allowance under 37 CFR § 1.312 which amended claims 14 and 38 “to address antecedent basis issues.” EX1006, 7. The Examiner entered the amendment in a Response to Rule 312 Communication sent on February 10, 2025. EX1006, 6. After sending the issue notification on February 19, 2025, the USPTO issued the 437 patent on March 11, 2025. EX1006, 1-4.

C. Person of Ordinary Skill in the Art

33. 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.

D. Claim Construction

34. Below are claim constructions that, in my opinion, would have been their ordinary and customary meaning according to a POSITA (person of ordinary skill in the art in question on December 5, 2019).

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

35. It is my opinion that a POSITA would have understood “fluidly coupled” in light of the specification to mean capable of being connected or linked together using a gas or liquid. 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.”).

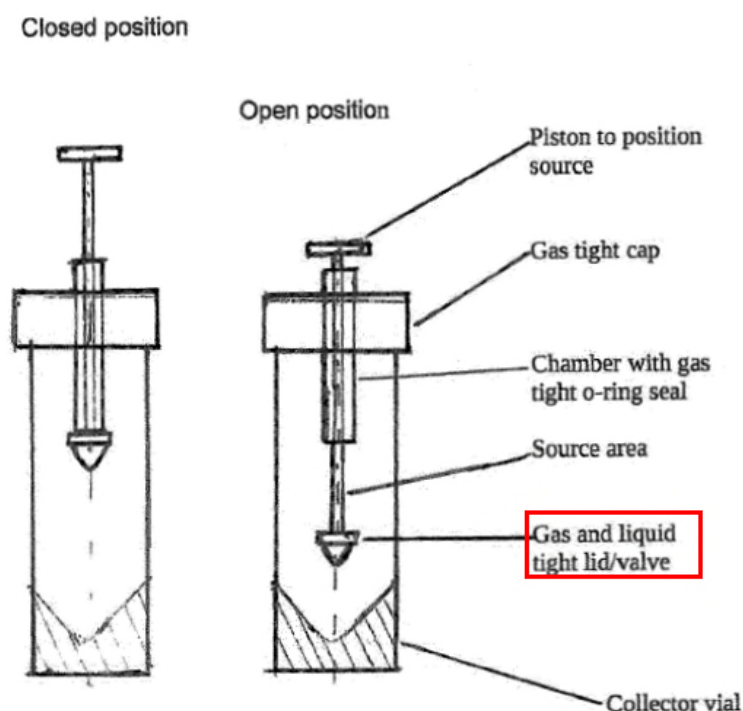
2. Limitation 1c construction - “wherein the solid precursor isotope source is configured to be fluidly coupled to a volume including a collector surface with a gas tight seal” (claim 1)

36. It is my opinion that 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.

37. 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.

38. Alternatively, under the second possible construction, a POSITA would have understood the limitation 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.

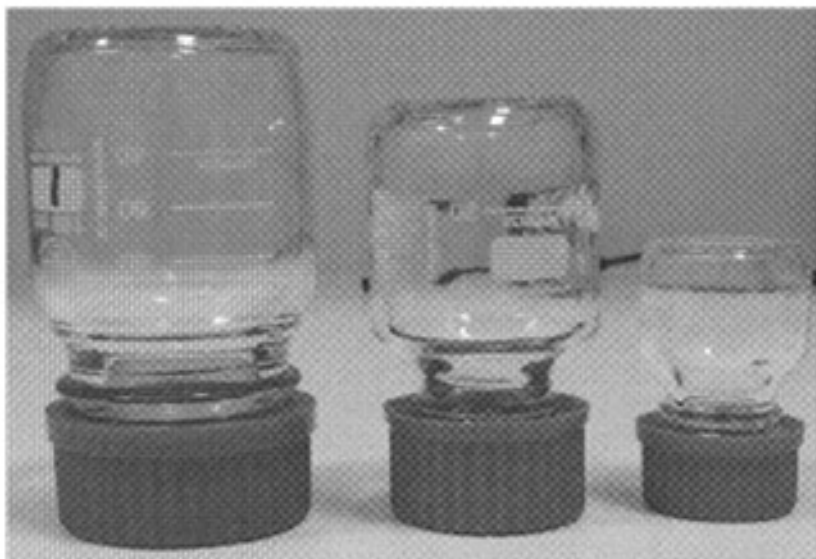


Fig. 5A

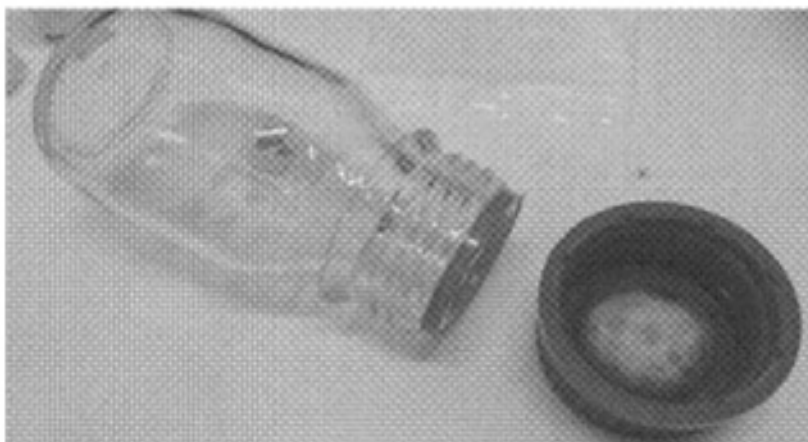


Fig. 5B

EX1001, Figs. 5A-B.

39. In the grounds below, I address these possible constructions, including the third construction.

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

40. It is my opinion that 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.

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

41. 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, in my opinion, a POSITA would have understood this term to include both a direct or an indirect physical connection.

5. “removably connect” (claim 11)

42. 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, in my opinion, a POSITA would have understood that the term “removably connect” includes both a direct or an indirect physical connection that is removable.

6. “with” (claim 34)

43. 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. Thus, in my opinion, a POSITA would have understood the word "with" to mean "that includes" in this limitation.

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

A. Hassfjell-Hoff

44. 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.

45. 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 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. Roy Larsen is listed as an inventor on EX1005 and EX1015. In my opinion, a POSITA would have understood that journals (e.g., EX1003) and published patent applications (e.g., EX1005) are reliable sources of information and would have been capable of accessing them well before the alleged filing date of the 437 patent. I have been informed that Hassfjell-Hoff qualifies as prior art under 35 U.S.C. §102(a).

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

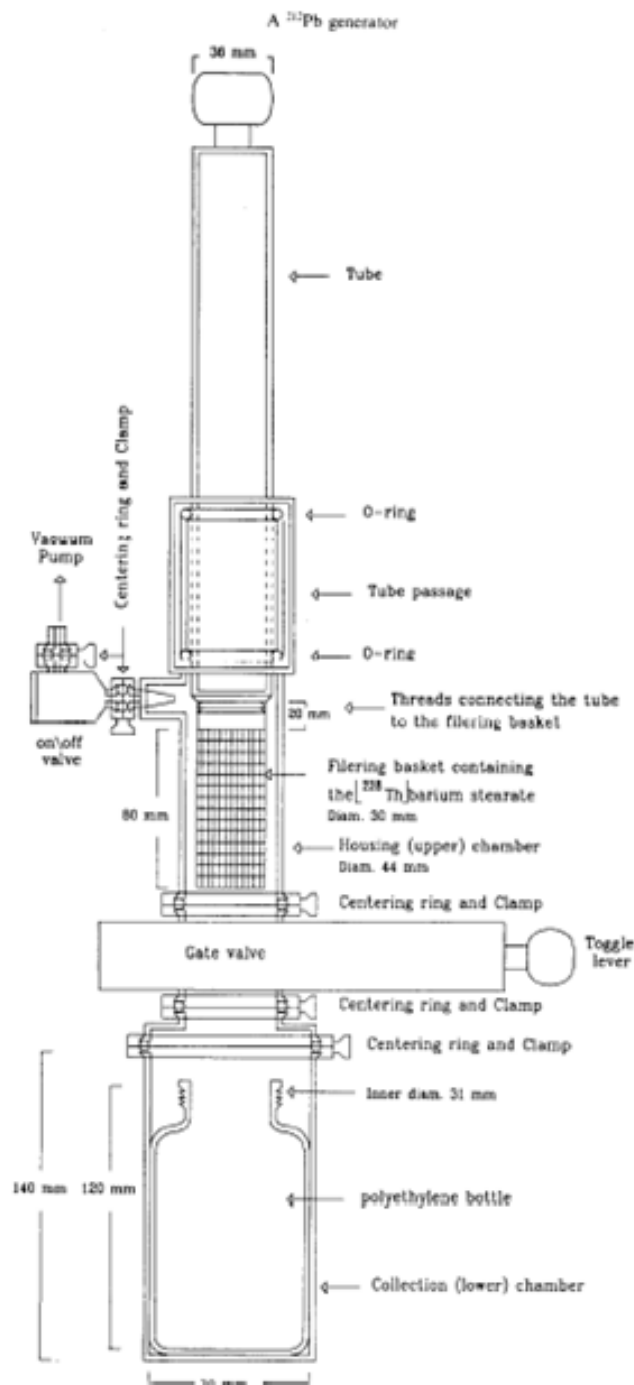


Fig. 2. The design of the generator showing functional details and operating mechanism.

EX1003, Fig. 2.

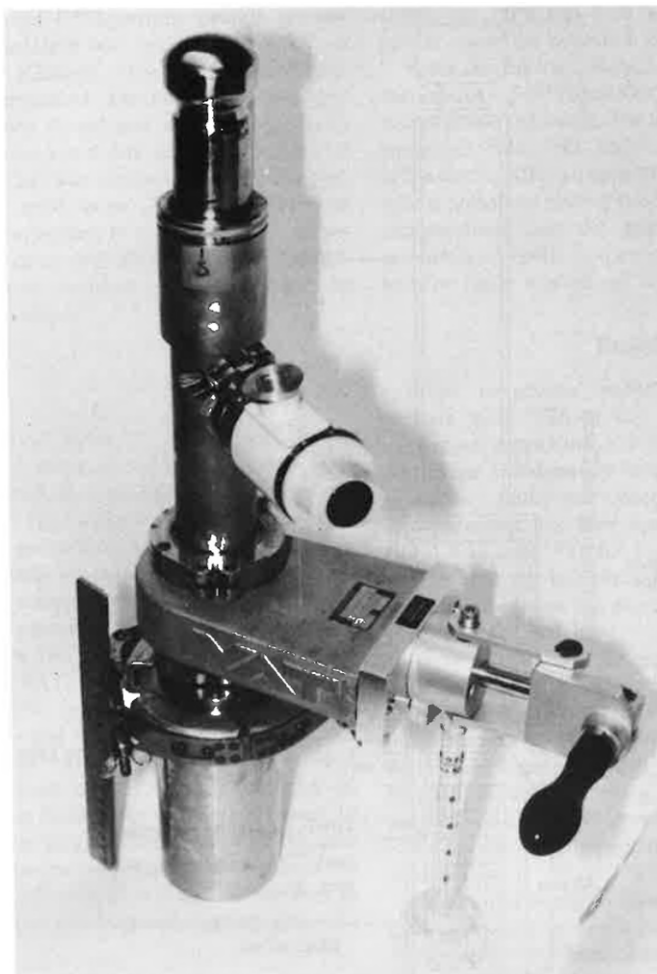


Fig. 3. A picture of the generator.

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 ,” namely “ ^{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, and the gate valve is closed. The polyethylene bottle is then removed, and the radioactivity easily washed off with a suitable solution.” EX1003, 7.

47. 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

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>.

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.

48. In my opinion, Hassfjell-Hoff is analogous art to the 437 patent. Hassfjell-Hoff is from the same field of endeavor as the 437 patent. They are both in the field of radioisotope generators. *See* EX1001, 1:20-27 (describing diffusion generators and methods for obtaining a container comprising the ^{212}Pb radioisotope); EX1003, 6 (describing various prior art generators for obtaining ^{212}Pb by the natural decay of ^{220}Rn gas in a collection chamber). In addition, Hassfjell-Hoff is reasonably relevant to the problem the 437 patent is concerned with, as shown in my analysis below in Sections IV(B)-(CC).

49. As I explain below, it was material error for certain claims of the 437 patent to issue over Hassfjell-Hoff.

B. Claim 1

50. In my opinion, Hassfjell-Hoff discloses this claim arranged as claimed and in an enabling manner and renders this claim obvious.

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

51. In my opinion, 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.

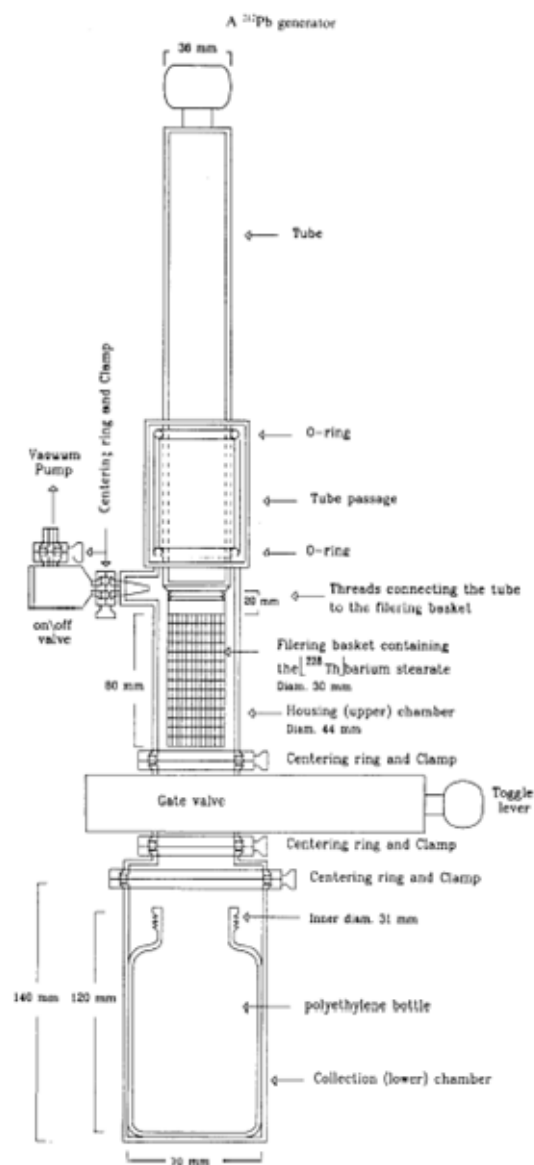


Fig. 2. The design of the generator showing functional details and operating mechanism.

EX1003, Fig. 2.

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

52. In my opinion, Hassfjell-Hoff discloses this limitation. Hassfjell-Hoff discloses that the radioisotope generator includes a *solid precursor isotope source* (i.e., packet of [^{228}Th]barium stearate). See EX1003, Abstract, 7. The *precursor isotope source* is prepared by a known method that results in the [^{228}Th]barium stearate being precipitated from a solution onto a filter membrane. EX1003, 6-7. Hassfjell-Hoff’s “Gelman, U.S.” filter membrane with the [^{228}Th]barium stearate precipitate is a *solid* that is formed into packets. EX1003, 7. In my opinion, 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 [^{228}Th]barium stearate precipitate is formed into the membrane packet, it forms a solid.

53. In my opinion, Hassfjell-Hoff further discloses that the *solid precursor isotope source* (i.e., packet of [^{228}Th]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 [^{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.

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.

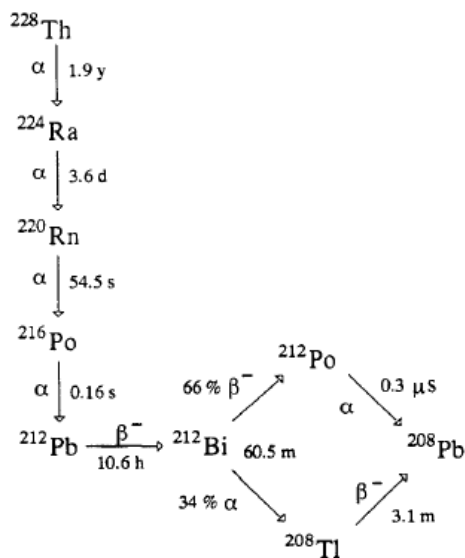


Fig. 1. The decay mode of ^{228}Th to stable ^{208}Pb .

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.

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

54. In my opinion, 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.

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

55. In my opinion, 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).

56. 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).

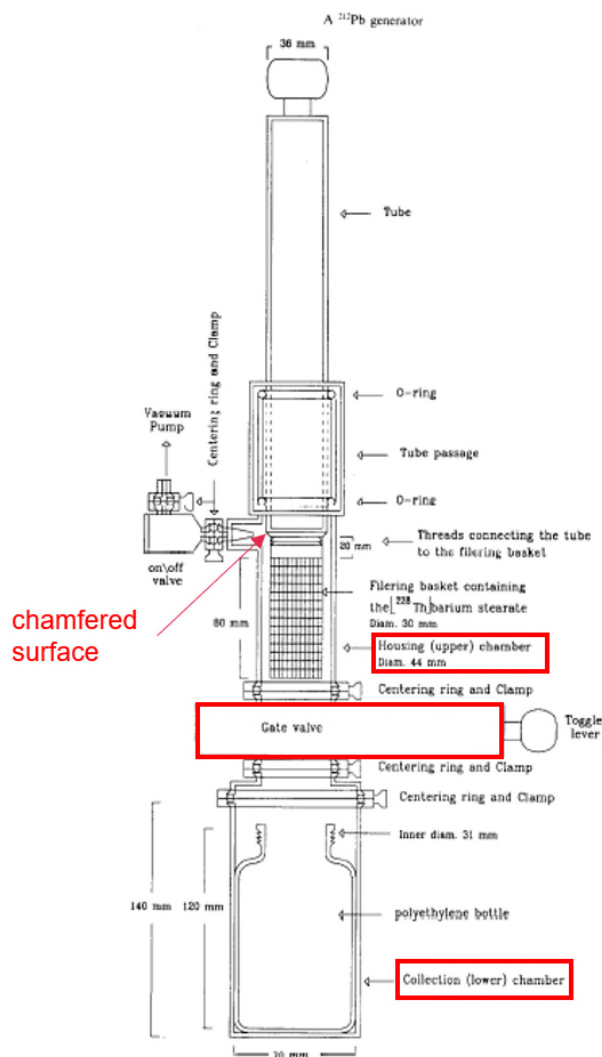


Fig. 2. The design of the generator showing functional details and operating mechanism.

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 ^{228}Th 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. A POSITA would have understood 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 polyethylene 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.

b. Third Construction

57. In my opinion, Hassfjell-Hoff additionally 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.

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.”

58. In my opinion, Hassfjell-Hoff discloses this limitation. Hassfjell-Hoff discloses that the *solid precursor isotope source* (*i.e.*, packet of [^{228}Th]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 ^{220}Rn) *deposit one or more solid progeny isotopes* (*i.e.*, ^{212}Pb and ^{212}Bi) *on the collector surface*:

When the tube is lowered, the filtering 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, 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 [^{228}Th]barium stearate becomes positioned inside the bottle such that gaseous ^{220}Rn (a progeny isotope of ^{228}Th) emanates from the source and solid progeny isotopes (^{212}Pb and ^{212}Bi) are deposited on the interior walls of the bottle (*i.e.*, the collector surface).

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

59. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 1. See §IV(B) (claim 1).*

60. In my opinion, 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 “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.” 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.

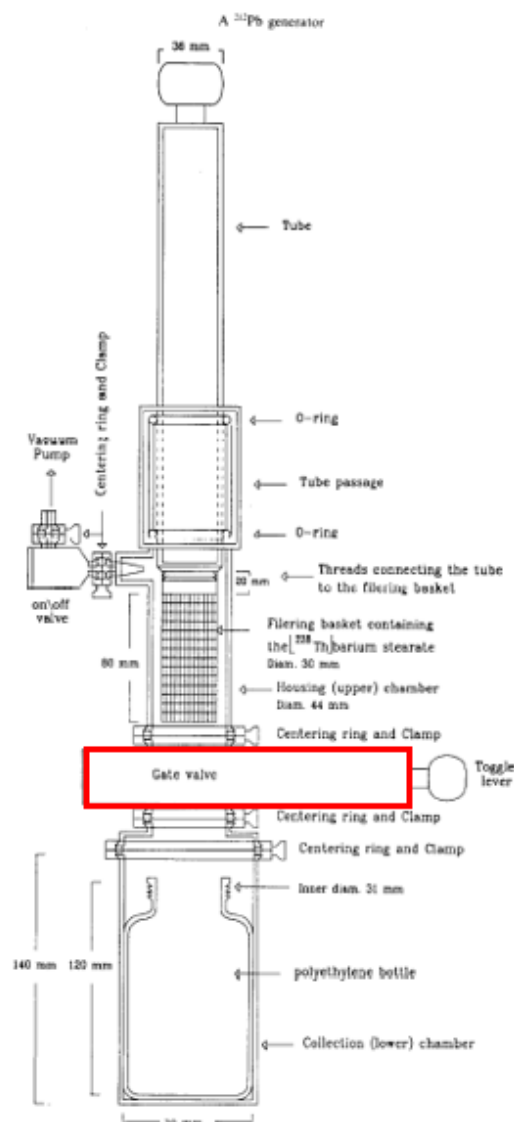


Fig. 2. The design of the generator showing functional details and operating mechanism

EX1003, Fig. 2.

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

61. As I explained above, Hassfjell-Hoff discloses and renders obvious the radioisotope generator of claim 1. See §IV(B) (claim 1).

62. In my opinion, 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 in turn is attached to the lower chamber (i.e., *volume*) via the gate valve:

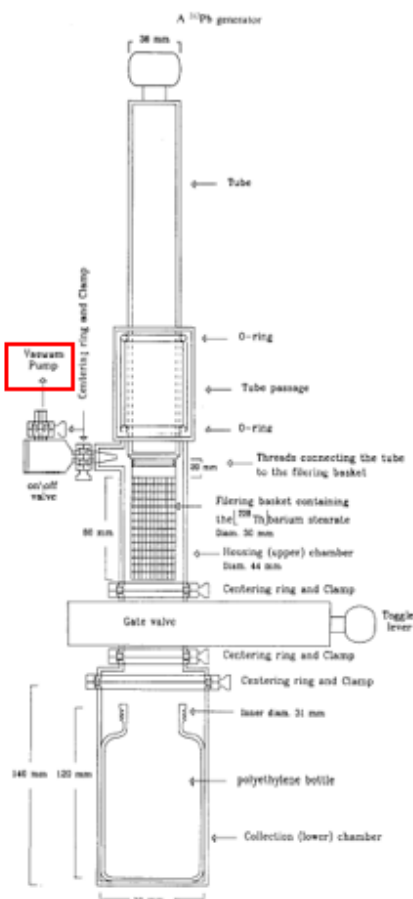


Fig. 2. The design of the generator showing functional details and operating mechanism.

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

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).”

63. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 1. See §IV(B) (claim 1).*

64. In my opinion, 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.

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."

65. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 1. See §IV(B) (claim 1).*

66. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner and renders them obvious. 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 and renders obvious the gate valve being a gas tight seal. Alternatively, as shown above in Section IV(B)(4) (limitation 1c), Hassfjell-Hoff renders obvious a gas tight seal between the tube and the polyethylene bottle.

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.”

67. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 8. See §§IV(B), (F) (claims 1, 8).*

68. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner and renders them obvious. *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:*

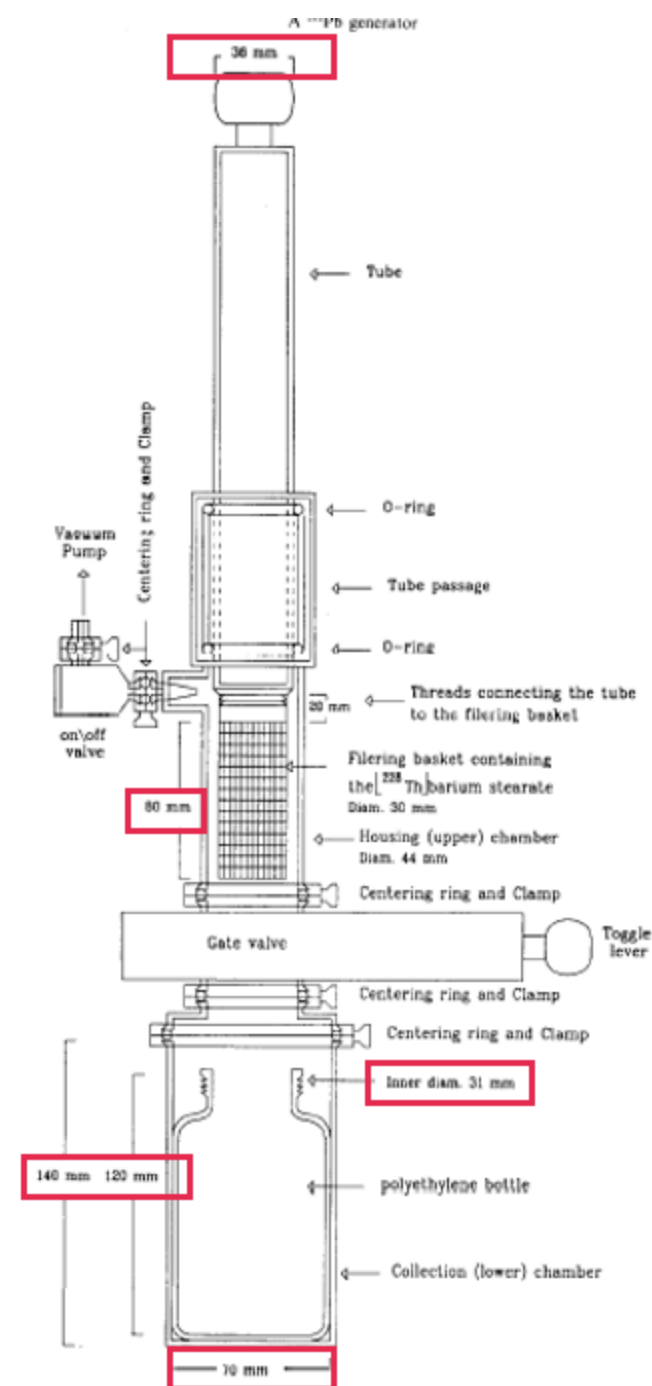


Fig. 2. The design of the generator showing functional details and operating mechanism.

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 [^{228}Th]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).

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

69. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 8*. See §§IV(B), (F) (claims 1, 8).

70. In my opinion, 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.

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

71. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 10*. See §§IV(B), (F), (H) (claims 1, 8, 10).

72. In my opinion, 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).

73. 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 ^{228}Th 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.

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.”

74. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 10. See §§IV(B), (F), (H) (claims 1, 8, 10).*

75. In my opinion, 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.”). A POSITA would have understood that an example of increasing the ionic strength of the washing solution is using a dilute acid rather than distilled water. A POSITA would have understood that the “chelating agent” is a chelator. The chelating agent is disposed on the walls of the bottle (*i.e.*, the interior surface) and is configured to chelate the one or more solid progeny isotopes (*i.e.*, ^{212}Pb) from the interior surface.

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.”

76. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 10. See §§IV(B), (F), (H) (claims 1, 8, 10).*

77. In my opinion, 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., a 1.0 M solution of NaCl or a solution of NaCl having a concentration of 1.0 M) 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 solution, 99% of the ^{212}Pb can be washed of the walls of the bottle.”). The volume is configured to receive 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*). In my opinion, 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” (EX1003, 7), and Norman similarly discloses that “the open porosity medium can be dissolved in water in order to obtain a solution whose principal radioactivity results from the daughter isotopes.” EX1007, 4:1-4. *See also* 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). In my opinion, 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.

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.”

78. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 1. See §IV(B) (claim 1).*

79. In my opinion, 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.

M. Claim 16

80. In my opinion, Hassfjell-Hoff discloses this claim arranged as claimed and in an enabling manner and renders this claim obvious.

2. [16pre] “A method of generating a progeny radioisotope, the method comprising:”

81. In my opinion, 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.

3. [16a] “allowing one or more gaseous progeny isotopes to emanate from a solid precursor isotope source”

82. In my opinion, 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 filtering basket mounted by threads to the end of a long tube closed in both ends. The filtering 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 filtering 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.

EX1003, 7.

4. [16b] “the solid precursor isotope source comprising a precursor isotope”

83. In my opinion, Hassfjell-Hoff discloses this limitation. *See* §IV(B)(3) (limitation 1b).

5. [16c] “fluidly coupling a volume including a collector surface to the solid precursor isotope source using a gas tight seal; and”

84. In my opinion, Hassfjell-Hoff discloses and renders obvious 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). Alternatively, Hassfjell-Hoff discloses and renders obvious lowering the tube so that the filtering basket is placed into the polyethylene bottle and the chamfered surface near the bottom of the tube forms a gas-tight seal with the bottle opening. *See* §IV(B)(4) (limitation 1c).

85. 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.

6. [16d] “allowing one or more solid progeny isotopes of the one or more gaseous progeny isotopes to deposit on the collector surface.”

86. In my opinion, Hassfjell-Hoff discloses this limitation. Hassfjell-Hoff discloses *allowing one or more solid progeny isotopes (i.e., ^{212}Pb) 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).*

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

87. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 16. See §IV(M) (claim 16).*

88. In my opinion, 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.”).

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.”

89. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 16*. See §IV(M) (claim 16).

90. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner and renders them obvious. Hassfjell-Hoff discloses and renders obvious this claim. 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.

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

91. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 16*. See §IV(M) (claim 16).

92. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim as claimed and in an enabling manner and renders them obvious. 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.”).

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).”

93. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 16*. See §IV(M) (claim 16).

94. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(E) (claim 7).

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.”

95. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 16*. See §IV(M) (claim 16).

96. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(F) (claim 8).

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

97. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 23. See §§IV(M), (R) (claims 16, 23).*

98. In my opinion, 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).*

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

99. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 23. See §§IV(M), (R) (claims 16, 23).*

100. In my opinion, 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).* Th-228 is a solid precursor isotope disposed in the source. EX1003, 7 (“The desired [²²⁸Th]barium stearate precipitated from the solution”).

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.”

101. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 23. See §§IV(M), (R) (claims 16, 23).*

102. In my opinion, 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.”).*

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.”

103. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 23. See §§IV(M), (R) (claims 16, 23).*

104. In my opinion, 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).

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.”

105. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 16. See* §IV(M) (claim 16).

106. In my opinion, 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).

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

107. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 18. See* §§IV(M), (O) (claims 16, 18).

108. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner and renders them obvious. 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.

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

109. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 16. See §IV(M) (claim 16).*

110. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner and renders them obvious. Th-228 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).

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.”

111. As I explained above, Hassfjell-Hoff discloses and renders obvious *the method of claim 23*. *See* §§IV(M), (R) (claims 16, 23).

112. As I explain below, this claim is indefinite. *See* §XII(B).

113. I have been asked to address this claim under the assumption that Patent Owner argues that this claim should be construed to require “[t]he method of claim 23, *further comprising*.” Under this construction, in my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner and renders them obvious. *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.

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.”

114. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 3.* See §§IV(B)-(C) (claims 1, 3).

115. In my opinion, 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).

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

116. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 1.* See §IV(B) (claim 1).

117. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(Y) (claim 32). Th-228 is a solid precursor isotope disposed in the source. EX1003, 7 (“The desired [²²⁸Th]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).

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.”

118. As I explained above, Hassfjell-Hoff discloses and renders obvious *the radioisotope generator of claim 10*. See §§IV(B), (F), (H) (claims 1, 8, 10).

119. In my opinion, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(Z) (claim 34).

V. GROUND 2: CLAIMS 1, 3, 5-7, 15-16, 18, 20-22, 29-33, AND 35-37 ARE ANTICIPATED AND RENDERED OBVIOUS BY NORMAN

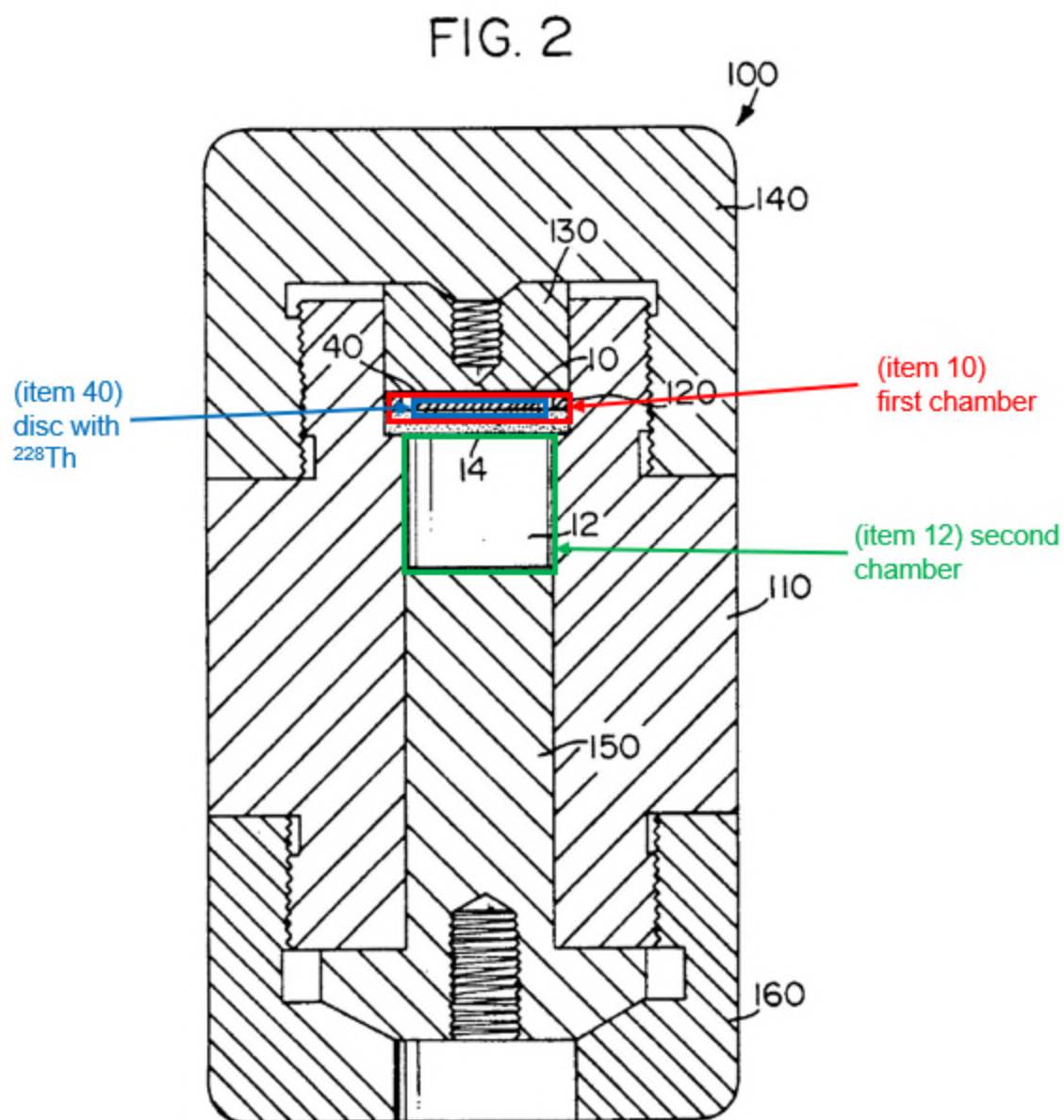
A. Norman

120. 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. I have been informed that O’Hara qualifies as prior art under 35 U.S.C. §102(a).

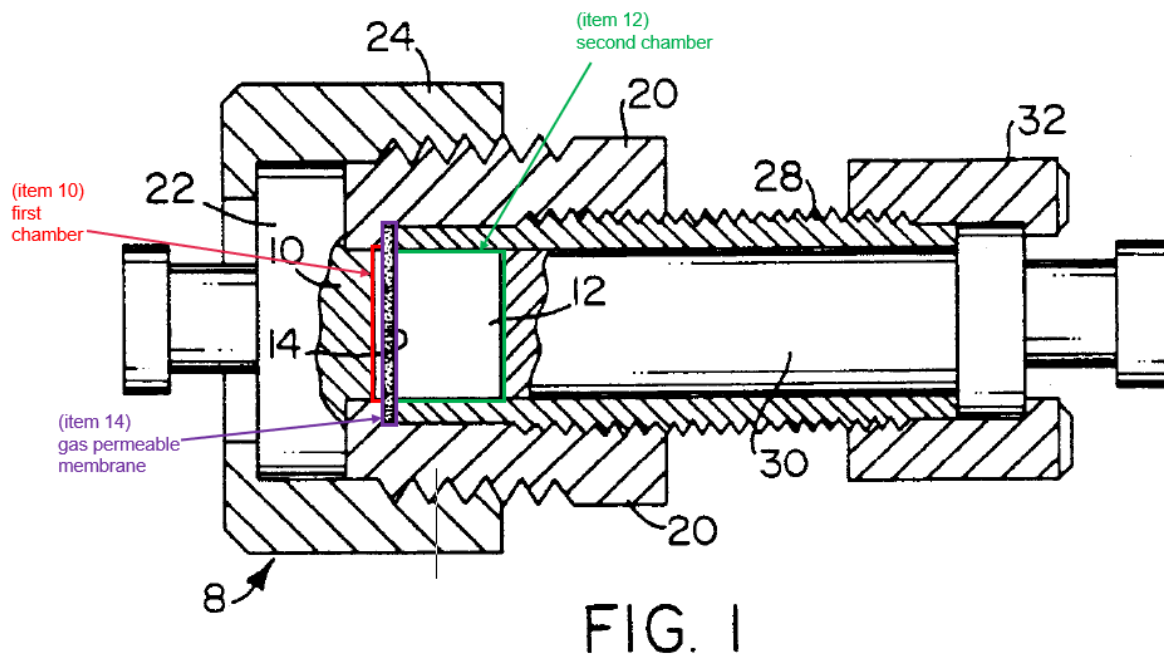
121. Norman discloses a method and generator for preparing the radioisotope of lead, ^{212}Pb , whereby ^{228}Th , in a closed first chamber 10, is allowed to decay to gaseous ^{220}Rn which is then readily separated from the thorium and other decay products by diffusing the ^{220}Rn gas into a second 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.

122. In my opinion, Norman is analogous art to the 437 patent. Norman is from the same field of endeavor as the 437 patent. They are both in the field of radioisotope generators. *See* EX1001, 1:20-27 (describing diffusion generators and methods for obtaining a container comprising ²¹²Pb radioisotope); EX1007, Abstract, 1:5-8. In addition, Norman is reasonably relevant to the problem the 437 patent is concerned with, as shown in my analysis below in Sections V(B)-(HH).

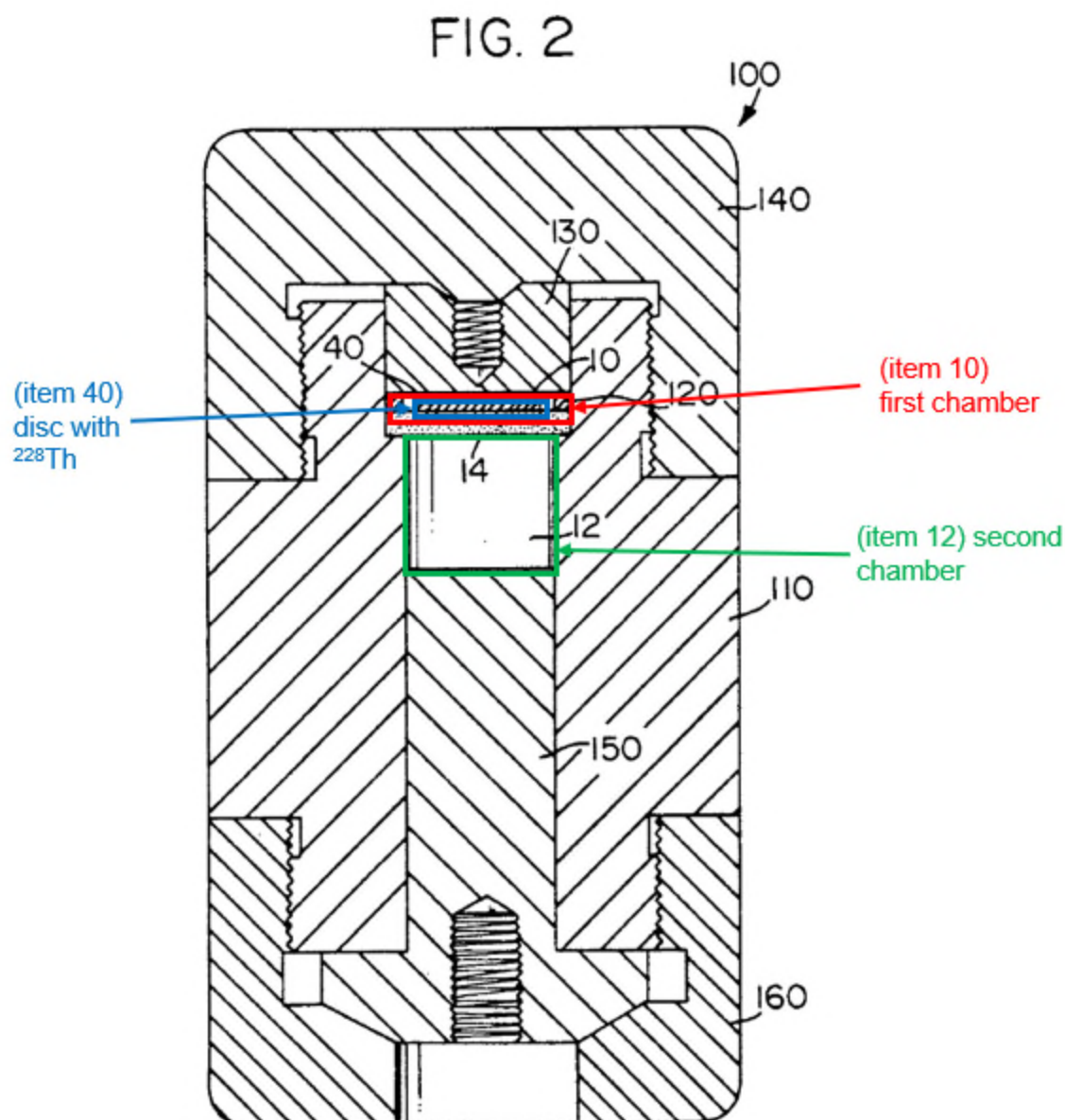
123. Moreover, as shown below, it was a material error for certain claims of the 437 patent to issue over Norman.

B. Claim 1

124. In my opinion, Norman discloses this claim arranged as claimed and in an enabling manner and renders this claim obvious.

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

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



EX1007, Fig. 2.

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

126. In my opinion, 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”).

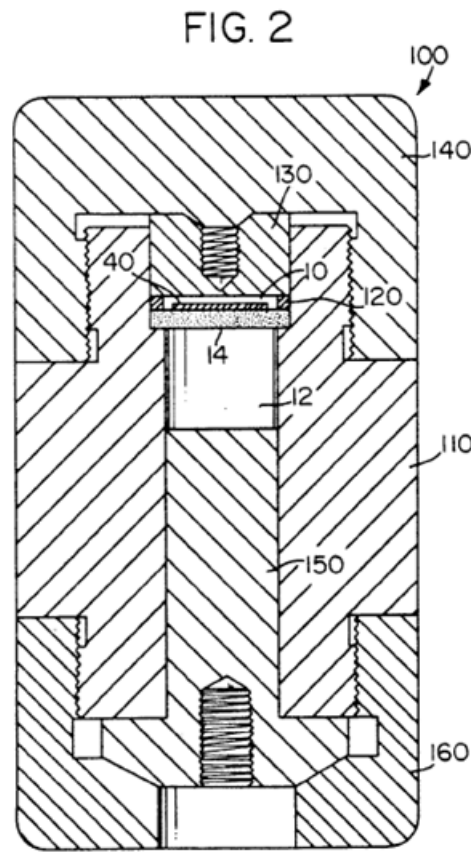
3. [1b] “the solid precursor isotope source comprising a precursor isotope; and”

127. In my opinion, 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 §V(B)(2) (limitation 1a).

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

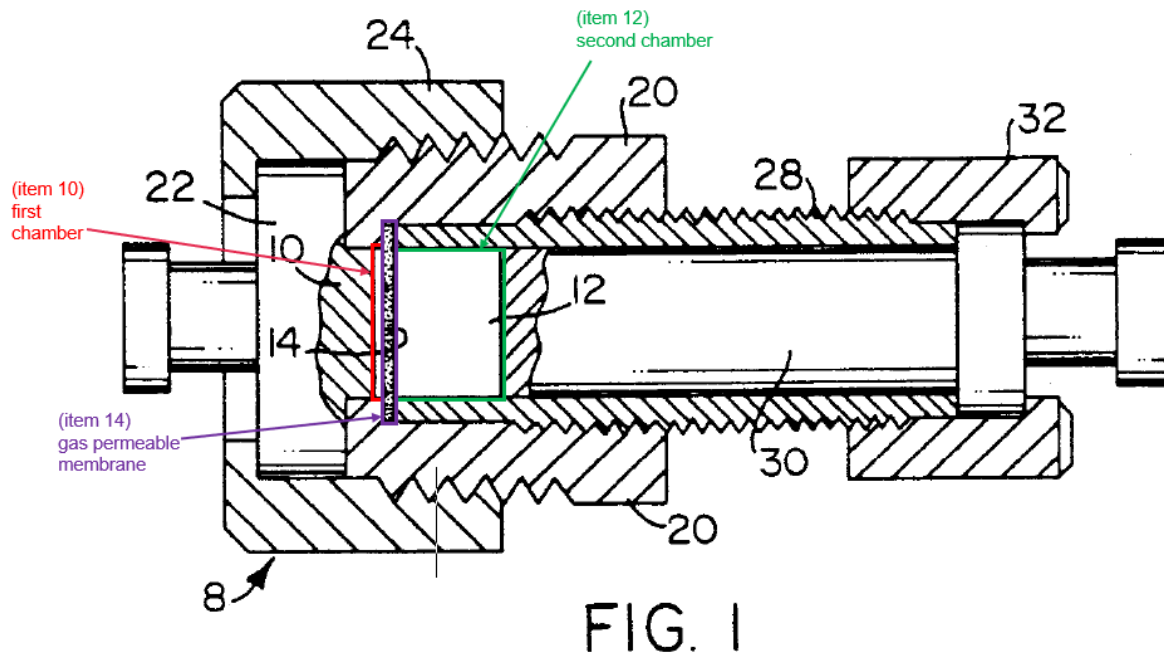
128. In my opinion, Norman discloses and renders obvious this limitation under either the first or second constructions of limitation 1c. See §§III(D)(1), (2) (constructions of “fluidly coupled” and limitation 1c). As shown in Figure 2, the solid precursor isotope source 40 is fluidly coupled to the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



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.”).

129. 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.

130. 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.

131. 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 (*i.e.*, the collecting chamber 12 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, Fig. 2.

132. To the extent Norman does not expressly disclose that Figure 2 has a gas-tight seal, 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.

a. Third Construction

133. Additionally, in my opinion, 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 ^{220}Rn 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.

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.”

134. In my opinion, 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.”).

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

135. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 1*. See §V(B) (claim 1).

136. In my opinion, 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 ²²⁰Rn diffuses from parental chamber 10 into the collection chamber 12.”).

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.”

137. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 1*. See §V(B) (claim 1).

138. In my opinion, 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.”).

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

139. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 5*. See §§V(B), (D) (claims 1, 5).

140. In my opinion, 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.”).

- 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).”**

141. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 1. See §V(B) (claim 1).*

142. In my opinion, Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See 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.”).*

- 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.”**

143. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 1. See §V(B) (claim 1).*

144. In my opinion, 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 ^{220}Rn diffuses from parental chamber 10 into the collection chamber 12.”).

H. Claim 16

145. In my opinion, Norman discloses this claim arranged as claimed and in an enabling manner and renders this claim obvious.

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

146. In my opinion, Norman discloses the preamble. *See* §V(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.”).

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

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

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

148. In my opinion, Norman discloses this limitation. *See* §V(B)(3) (limitation 1b).

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

149. In my opinion, Norman discloses this limitation and renders it obvious. *See* §V(B)(4) (limitation 1c).

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

150. In my opinion, Norman discloses this limitation. *See* §V(B)(5) (limitation 1d).

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.”

151. As I explained above, Norman discloses and renders obvious *the method of claim 16*. *See* §V(H) (claim 16).

152. In my opinion, 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; §V(C) (claim 3).

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

153. As I explained above, Norman discloses and renders obvious *the method of claim 16. See §V(H) (claim 16).*

154. In my opinion, Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See §V(D) (claim 5).*

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

155. As I explained above, Norman discloses and renders obvious *the method of claim 20. See §§V(H), (J) (claims 16, 20).*

156. In my opinion, Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See §V(E) (claim 6);* EX1007, 7:51-56.

- 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).”**

157. As I explained above, Norman discloses and renders obvious *the method of claim 16*. See §V(H) (claim 16).

158. In my opinion, Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §V(F) (claim 7); EX1007, Abstract.

- 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.”**

159. As I explained above, Norman discloses and renders obvious *the method of claim 16*. See §V(H) (claim 16).

160. In my opinion, Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §V(G) (claim 15). EX1007, 8:33-41.

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

161. As I explained above, Norman discloses and renders obvious *the method of claim 16*. See §V(H) (claim 16).

162. In my opinion, 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 ^{212}Pb 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.”).

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

163. As I explained above, Norman discloses and renders obvious *the method of claim 18*. See §§V(H)-(I) (claims 16, 18).

164. In my opinion, 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.

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

165. As I explained above, Norman discloses and renders obvious *the method of claim 16. See §V(H) (claim 16).*

166. In my opinion, 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. Th-228 is a solid disposed in the matrix. *See §V(B)(3) (limitation 1b).*

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

167. As I explained above, Norman discloses and renders obvious *the method of claim 32. See §§V(H), (P) (claims 16, 32).*

168. In my opinion, Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See §V(P) (claim 32).* EX1007, 7:51-64.

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.”

169. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 3. See §§V(B)-(C) (claims 1, 3).*

170. In my opinion, 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 §V(O) (claim 31).

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

171. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 1. See §V(B) (claim 1).*

172. In my opinion, Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See §V(P) (claim 32).*

Th-228 is a solid disposed in the matrix. *See §V(B)(3) (limitation 1b).*

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

173. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 36. See §§V(B), (S) (claims 1, 36).*

174. In my opinion, Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See §V(Q) (claim 33).*

VI. GROUND 3: CLAIMS 1, 3-12, 14-26, AND 28-38 ARE OBVIOUS OVER HASSEFJELL-HOFF AND NORMAN

A. Hassfjell-Hoff

175. My explanation of the Hassfjell-Hoff reference is above and incorporated here by reference into Ground 3. *See §IV(A).*

B. Norman

176. My explanation of the Norman reference is above and incorporated here by reference into Ground 3. *See* §V(A).

C. Motivation to Combine

177. To the extent that the gas-tight seal is construed as modifying the volume (*See* §III(D)(2) (second 1c construction)), in my opinion, 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 modify Hassfjell-Hoff such that its tube forms a gas-tight seal with 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.

178. Specifically, in my opinion, 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.

179. Moreover, in my opinion, 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.

180. Further, in my opinion, 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.

D. Claim 1

181. In my opinion, Hassfjell-Hoff and Norman render this claim obvious.

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.”

182. In my opinion, Hassfjell-Hoff discloses these limitations. *See* §§IV(B)(1)-(3), (5) (limitations 1pre, 1a, 1b, 1d).

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”**

183. As explained above, this limitation is disclosed by Hassfjell-Hoff (§IV(B)(4) (limitation 1c)) and is disclosed by Norman (§V(B)(4) (limitation 1c)).

184. Moreover, in my opinion, 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* §VI(C) (motivation to combine).

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

185. As I explained above, Hassfjell-Hoff in view of Norman renders obvious claim 1. *See* §VI(D) (claim 1).

186. As I 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.

F. Claim 16

187. In my opinion, Hassfjell-Hoff in view of Norman renders this claim obvious. *See* §IV(M); §V(H); §VI(D).

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

188. As I explained above, Hassfjell-Hoff in view of Norman renders obvious claim 16. *See* §VI(F) (claim 16).

189. As I explained above, the additional limitations of these claims are disclosed by Hassfjell-Hoff. *See* §§IV(N)-(Z), (CC) (claims 17-19, 22-26, 28-29,

31-32, and 34). Therefore, these claims are rendered obvious by Hassfjell-Hoff in view of Norman.

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

190. As I explained above, these claims are disclosed and rendered obvious by Norman. *See* §§V(D)-(E), (J)-(K), (Q), (T) (claims 5-6, 20-21, 33, and 37).

191. Moreover, these limitations are obvious by Hassfjell-Hoff in view of Norman. *See* §§VI(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* §VI(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* §VI(C)(2) (motivation to combine). A POSITA would have known that the precursor isotope would be encapsulated by the porous material. *See* §VI(C)(2) (motivation to combine).

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

192. As explained above, this claim is disclosed and rendered obvious by Norman. *See* §V(N) (claim 30).

193. Moreover, in my opinion, claim 30 is obvious by Hassfjell-Hoff in view of Norman. 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* §VI(C) (motivation to combine).

VII. GROUND 4: CLAIM 2 IS OBVIOUS OVER HASSFJELL-HOFF AND IAEA

A. Hassfjell-Hoff

194. My explanation of the Hassfjell-Hoff reference is above and incorporated here by reference into Ground 4. *See* §IV(A).

B. IAEA

195. 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.

196. 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.

197. I have been informed that IAEA qualifies as prior art under 35 U.S.C. §102(a).

198. 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:

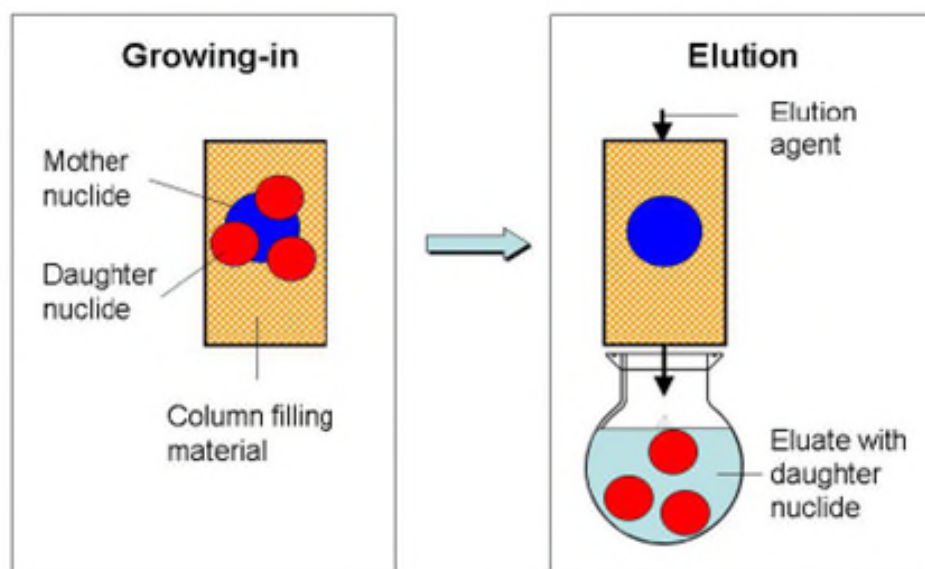


FIG 6. Principle of a column based radionuclide generator.

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

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

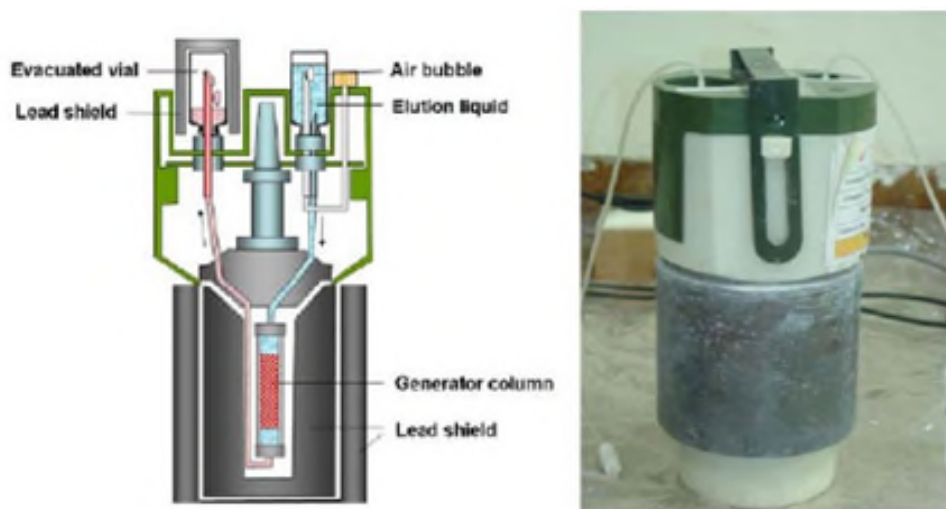


FIG 19. Left: A column generator in its lead shield. Elution is performed by a vacuum vial, also in a lead shield. Right: A typical lead-shielded and closed radionuclide generator.

EX1008, Fig. 19.

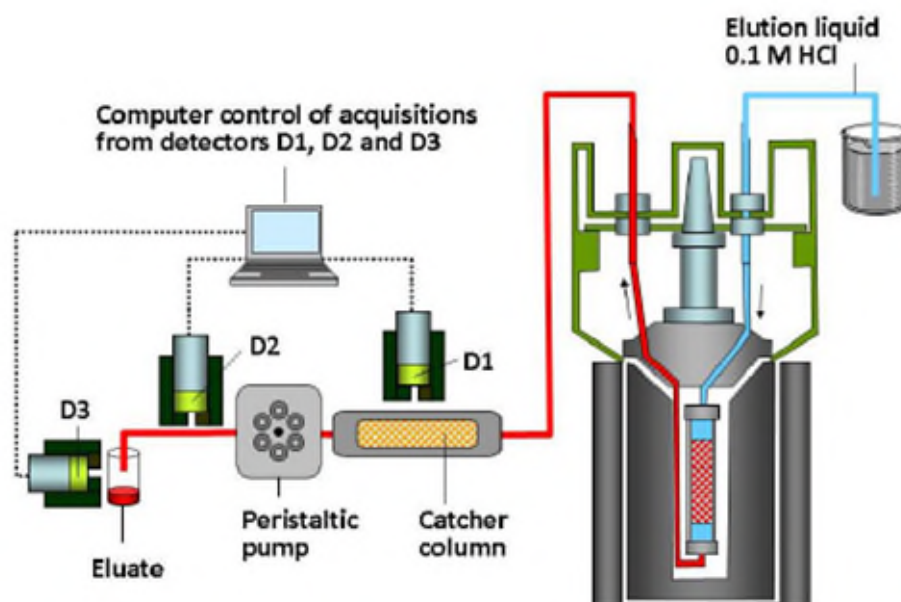


FIG 20. A generator set-up that is eluted by means of a peristaltic vacuum pump and with a catcher column outside the main generator housing for easy detection of mother radionuclide breakthrough.

EX1008, Fig. 20.

200. 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.

201. In my opinion, IAEA is analogous art to the 437 patent. IAEA is from the same field of endeavor as the 437 patent. They are both in the field of radioisotope generators. *See* EX1001, 1:20-27 (describing diffusion generators and methods for obtaining a container comprising ^{212}Pb radioisotope); EX1008, 20-24 (describing radionuclide generator properties), 24-25 (describing types of radionuclide generators), 47-50 (describing radiotracer generators based on radionuclide generators), Figs. 6, 19, and 20. In addition, IAEA is reasonably relevant to the problem the 437 patent is concerned with, as shown in my analysis below in Section VII(C).

202. 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.

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

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

204. 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* §VII(B). IAEA discloses numerous examples of radionuclide generators that include an elution agent provided via a flushing circuit. EX1008, Figs. 6, 19, and 20.

205. In my opinion, 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.

VIII. GROUND 5: CLAIMS 13 AND 27 ARE OBVIOUS OVER HASSFJELL-HOFF AND WESTRØM

A. Hassfjell-Hoff

206. My explanation of the Hassfjell-Hoff reference is above and incorporated here by reference into Ground 5. *See* §IV(A).

B. Westrøm

207. 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.

208. 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.

209. I have been informed that Westrøm qualifies as prior art under 35 U.S.C. §102(a).

210. 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. In other words, a POSITA would have understood that TCMC has become a chelating agent of choice forming a more stable complex.

211. In my opinion, Westrøm is analogous art to the 437 patent. Westrøm is from the same field of endeavor as the 437 patent. They are both in the field of generating radioisotopes. *See* EX1001, 1:20-27 (describing diffusion generators and methods for obtaining a container comprising ^{212}Pb radioisotope); EX1009, 4-5. In addition, Westrøm is reasonably relevant to the problem the 437 patent is

concerned with, as shown in my analysis below in Sections VIII(C)-(D), IX(C)-(D), and X(D).

212. 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 and Norman in view of Westrøm.

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

213. Hassfjell-Hoff discloses and renders obvious claim 12. *See* §§IV(B), (F), (H), (J) (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.”). In other words, a POSITA would have understood that TCMC has become a chelating agent of choice forming a more stable complex.

214. In my opinion, 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, in my opinion, Hassfjell-Hoff in view of Westrøm renders claim 13 obvious.

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

215. In my opinion, Hassfjell-Hoff in view of Westrøm renders claim 27 obvious. *See* §VIII(C) (claim 13); §§IV(M), (R), (U) (claims 16, 23, 26).

IX. GROUND 6: CLAIMS 8-12, 14, 17, 23-26, 28, 34, AND 38 ARE OBVIOUS OVER NORMAN AND HASSFJELL-HOFF

A. Norman

216. My explanation of the Norman reference is above and incorporated here by reference into Ground 6. *See* §V(A).

B. Hassfjell-Hoff

217. My explanation of the Hassfjell-Hoff reference is above and incorporated here by reference into Ground 6. *See* §IV(A).

C. Motivation to Combine

1. Hassfjell-Hoff’s container surface with Norman

218. In my opinion, 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. EX1007, 3:4-11. Hassfjell-Hoff, which was published later and cites to Norman (EX1003, 6, 10), teaches collecting ^{212}Pb on an interior container surface. EX1003, 7.

219. Further, in my opinion, 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.

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

220. In my opinion, 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.

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

221. In my opinion, 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.

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

222. In my opinion, 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.

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.”

223. In my opinion, claim 8 is obvious by Norman in view of Hassfjell-Hoff.

224. As I explained above, Norman discloses and renders obvious *the radioisotope generator of claim 1*. See §V(B) (claim 1).

225. Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(F) (claim 8). As I explained above, in my opinion, 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 §IX(C)(1) (motivation to combine). Therefore, Norman in view of Hassfjell-Hoff renders claim 8 obvious.

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.”

226. In my opinion, claim 9 is obvious by Norman in view of Hassfjell-Hoff.

227. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the radioisotope generator of claim 8*. See §IX(D) (claim 8).

228. 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. Therefore, Norman in view of Hassfjell-Hoff renders claim 9 obvious.

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

229. In my opinion, claim 10 is obvious by Norman in view of Hassfjell-Hoff.

230. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the radioisotope generator of claim 8*. See §IX(D) (claim 8).

231. 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.

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

232. In my opinion, claim 11 is obvious by Norman in view of Hassfjell-Hoff.

233. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the radioisotope generator of claim 10*. See §§IX(D), (F) (claims 8, 10).

234. 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.

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.”

235. In my opinion, claim 12 is obvious by Norman in view of Hassfjell-Hoff.

236. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the radioisotope generator of claim 10*. See §§IX(D), (F) (claims 8, 10).

237. 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.”). As such, in my opinion, 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.

238. Alternatively, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(J)

(claim 12). In my opinion, 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* §IX(C)(2) (motivation to combine).

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.”

239. In my opinion, claim 14 is obvious by Norman in view of Hassfjell-Hoff.

240. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the radioisotope generator of claim 10*. *See* §§IX(D), (F) (claims 8, 10).

241. 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.”).

242. Alternatively, as I explained above, Hassfjell-Hoff discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(K) (claim 14). Hassfjell-Hoff discloses that a volume is configured to receive a solvent. *See* §IV(K) (claim 14). As such, in my opinion, 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* §IX(C)(3) (motivation to combine).

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

243. In my opinion, claim 17 is obvious by Norman in view of Hassfjell-Hoff.

244. As I explained above, Norman renders obvious *the method of claim 16*. *See* §V(H) (claim 16).

245. Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(N) (claim 17). In my opinion, a POSITA would have been motivated to modify Norman to flush the collector surface as taught by Hassfjell-Hoff. *See* §IX(C)(4) (motivation to combine).

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.”

246. In my opinion, claim 23 is obvious by Norman in view of Hassfjell-Hoff.

247. As I explained above, Norman renders obvious *the method of claim 16*. See §V(H) (claim 16).

248. Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. See §IV(R) (claim 23), §IX(D) (claim 8). In my opinion, 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 §IX(D) (claim 8); §IX(C)(1) (motivation to combine).

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

249. In my opinion, claim 24 is obvious by Norman in view of Hassfjell-Hoff.

250. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the method of claim 23*. See §IX(K) (claim 23).

251. 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* §§IX(E), (G) (claims 9, 11).

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

252. In my opinion, claim 25 is obvious by Norman in view of Hassfjell-Hoff.

253. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the method of claim 23*. *See* §IX(K) (claim 23).

254. 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* §IX(G) (claim 11).

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.”

255. In my opinion, claim 26 is obvious by Norman in view of Hassfjell-Hoff.

256. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the method of claim 23*. *See* §IX(K) (claim 23).

257. Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IX(H) (claim 12). In my

opinion, 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.

258. Alternatively, as explained above, Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed in an enabling manner. *See* §IX(H) (claim 12). In my opinion, 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* §IX(H) (claim 12); §IX(C)(2) (motivation to combine).

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.”

259. In my opinion, claim 28 is obvious by Norman in view of Hassfjell-Hoff.

260. As I explained above, Norman in view of Hassfjell-Hoff renders obvious *the method of claim 23*. *See* §IX(K) (claim 23).

261. Hassfjell-Hoff further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. *See* §IV(V) (claim 28). In my opinion, 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. §IX(C)(3) (motivation to combine).

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.”

262. In my opinion, claim 34 is obvious by Norman in view of Hassfjell-Hoff.

263. In my opinion, this claim is indefinite. *See* §XII(B).

264. To the extent Patent Owner argues that this claim should be construed to require “[t]he method of claim 23, ***further comprising***,” as I explained above, Norman in view of Hassfjell-Hoff renders obvious *the method of claim 23*. *See* §IX(K) (claim 23).

265. Norman further discloses the additional limitations of this claim arranged as claimed and in an enabling manner. Norman’s system includes a “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 stopcock is closed there are two separate chambers. Thus, opening the stopcock *form[s] ...a single chamber*.

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.”

266. In my opinion, claim 38 is obvious by Norman in view of Hassfjell-Hoff.

267. As I explained above, Norman in view of Hassfjell-Hoff discloses *the radioisotope generator of claim 10*. See §IX(D), (F) (claims 8, 10).

268. 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 §IX(P) (claim 34).

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

A. Norman

269. My explanation of the Norman reference is above and incorporated here by reference into Ground 7. See §V(A).

B. Hassfjell-Hoff

270. My explanation of the Hassfjell-Hoff reference is above and incorporated here by reference into Ground 7. See §IV(A).

C. Westrøm

271. My explanation of the Westrøm reference is above and incorporated here by reference into Ground 7. See §VIII(B).

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

272. In my opinion, claim 13 is obvious by Norman in view of Hassfjell-Hoff and Westrøm.

273. As I explained above, Norman in view of Hassfjell-Hoff discloses *the radioisotope generator of claim 12*. See §IX(H) (claim 12).

274. 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 ^{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.”). EX1009, 5. In other words, a POSITA would have understood that TCMC has become a chelating agent of choice forming a more stable complex.

275. In my opinion, 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, in my opinion, Norman in view of Hassfjell-Hoff and Westrøm renders claim 13 obvious.

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

276. In my opinion, claim 27 is obvious by Norman in view of Hassfjell-Hoff and Westrøm.

277. As I explained above, Norman in view of Hassfjell-Hoff discloses *the method of claim 26*. See §IX(N) (claim 26).

278. 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 §X(D) (claim 13).

XI. GROUND 8: CLAIMS 13 AND 27 ARE OBVIOUS OVER HASSFJELL-HOFF, NORMAN AND WESTRØM

A. Hassfjell-Hoff

279. My explanation of the Hassfjell-Hoff reference is above and incorporated here by reference into Ground 8. See §IV(A).

B. Norman

280. My explanation of the Norman reference is above and incorporated here by reference into Ground 8. See §V(A).

C. Westrøm

281. My explanation of the Westrøm reference is above and incorporated here by reference into Ground 8. *See* §VIII(B).

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

282. In my opinion, claim 13 is obvious by Hassfjell-Hoff in view of Norman and Westrøm.

283. As I explained above, Hassfjell-Hoff in view of Norman discloses *the radioisotope generator of claim 12*. *See* §VI(E) (claim 12).

284. 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.”). EX1009, 5. In other words, a POSITA would have understood that TCMC has become a chelating agent of choice forming a more stable complex.

285. In my opinion, 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, in my opinion, Norman in view of Hassfjell-Hoff and Westrøm renders claim 13 obvious.

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

286. In my opinion, claim 27 is obvious by Hassfjell-Hoff in view of Norman and Westrøm.

287. As I explained above, Hassfjell-Hoff in view of Norman discloses *the method of claim 26*. See §VI(G) (claim 26).

288. 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 §XI(D) (claim 13).

XII. GROUND 9: CLAIMS 1-15 AND 34-38 ARE UNPATENTABLE UNDER 35 U.S.C. §112

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

289. 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.

In my opinion, a POSITA reading the 437 patent would be unable to determine the scope of the claims with reasonable certainty. I have been informed that if a POSITA reading the 437 patent would be unable to determine the scope of the claims with reasonable certainty, the claims are indefinite.

290. I have been informed that because independent claim 1 is indefinite, dependent claims 2-15 and 35-38 are indefinite.

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

291. 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. I have been informed that if a POSITA reading the 437 patent would be unable to determine the scope of the claims with reasonable certainty, the claims are indefinite. In my opinion, a POSITA is not able to determine the intended scope of claim 34.

XIII. SECONDARY CONSIDERATIONS

292. I am not aware of any relevant information related to secondary considerations of obviousness. For example, I am not aware of any attempt to commercialize the claimed technology in a product or through licensing. To the extent Patent Owner comes forward with any such information, I will consider it.

XIV. AVAILABILITY FOR CROSS-EXAMINATION

293. In signing this Declaration, I recognize that the Declaration will be filed as evidence in a contested case before the Patent Trial and Appeal Board of the United States Patent and Trademark Office. I also recognize that I may be subject to cross-examination in the case and that cross-examination will take place within the United States. If cross-examination is required of me, I will appear for cross-examination within the United States during a time as mutually agreed between the parties.

XV. RIGHT TO SUPPLEMENT

294. I reserve the right to supplement my opinions in the future to respond to any arguments that the Patent Owner raises. This Declaration represents only

those opinions that I have formed to date. I reserve the right to revise, supplement, and/or amend my opinions stated herein based on new information that becomes available to me and on my continuing analysis of the materials already provided.

XVI. CONCLUSION

295. I may utilize the documents cited and/or listed herein, or portions of those documents, as exhibits at any hearing or trial in this proceeding. I may further prepare and use exhibits that summarize portions of my testimony or key terms or concepts presented therein, or other demonstrative exhibits, at any hearing or trial in this proceeding.

296. I reserve the right to supplement my testimony and this report in response to any judicial determinations, in response to the arguments expressed by the Patent Owner or the opinions of the Patent Owner's experts in this proceeding, and/or in light of additional evidence or testimony brought forth at trial or otherwise brought to my attention after the date of my signature on the cover page.

APPENDIX 1

Biographical Sketch

Saed Mirzadeh

1039 Governor Dempsey Dr.,
Santa Fe, NM 87501-1045
email: saedmirzadeh@gmail.com,
cell phone: 865-599-6613

Education/Training:

National University of Iran, Tehran, Iran	B.S.	1969	Chemistry
University of New Mexico, Albuquerque, NM	Ph.D.	1979	Radiochemistry
Brookhaven National Laboratory, L.I., NY	Postdoc	1980	Nuclear Chemistry

Research and Professional Experience:

2021-present Consultant, Rdiomedix Inc., 9701 Richmond Avenue, Suite 222, Houston, TX 77042
 Consultant, Cardinal Health, 7200 Cardinal Pl., Dublin, OH 43017.

1989-2020 Distinguished Staff Scientist and ORNL Corporate fellow (retired 9/31/2020), Nuclear and Radiochemistry Group, Nuclear Security & Isotope Technology Division, Oak Ridge National Laboratory. *Research in radioisotope production, cross section measurements, neutron-induced reactions model calculations, mentor for MS and Ph.D. graduate students*

1993-1993 Visiting Scientist, Australian Nuclear Science and Technology. *Research on reactor production of medical radioisotopes*

1987-1989 Scientist, Radiation Oncology, National Cancer Institute, National Institutes of Health. *Research on radiometal labeling of antibodies.*

1985-1987 Adjunct Associate Professor of Chemistry, Natural Sciences Division, Long Island University. *Taught courses on Instrumental Analysis with an emphasis on neutron activation analysis*

1981-1987 Scientist, Medical Department, Brookhaven National Laboratory. *Research in radioisotope production, cross section measurements, charged particle-induced reactions*

1980-1981 Research Associate, Chemistry Department, Brookhaven National Laboratory. *Experimental Nuclear chemistry, synthesis of short-lived radionuclide far from stability.*

1979 Research Associate, Medical Radioisotope Program, Los Alamos National Laboratory. *Research on medical radioisotope production*

Selected Publications:

A. C. Peacock, R. Copping, J. R. Griswold, R. A. Boll, D. L. Denton, J. A. Gaugler, Widner, K. E. Murphy, D. Stracener. and S. Mirzadeh, "Separation of Radium from Barium and other Group II Elements Using Reverse Phase Cation Exchange Chromatography in Citrate Media" for submission to Radiochimica Acta (2024) (under DOE/ORNL internal review).

J. G. Mwakiseghe, G. Schweitzer and S. Mirzadeh, "Synthesis and Stability of Actinium-225 Endohedral Fullerenes, $^{225}\text{Ac}@C_{60}$ ", ACS Omega 5(42):27016-27025, October 2020, DOI:10.1021/acsomega.0c01659.

Selected Publications (cont.):

J. G. Mwakisege, G. Schweitzer and S. Mirzadeh, "Synthesis and Stability of Actinium-225 Endohedral Fullerenes, $^{225}\text{Ac}@C_{60}$ ", ACS Omega 5(42):27016-27025, October 2020, DOI:10.1021/acsomega.0c01659.

S. Mirzadeh, "Innovation, Impact and Strategic Importance of Alpha Emitting Radionuclides", Journal of Medical Imaging and Radiation Sciences, **50**, S6-S10 (2019).

J. R. Griswold, C. U. Jost, D. W. Stracener, S. H. Bruffey, D. Denton, M. Garland, L. Heilbronn, and S. Mirzadeh, "Production of ^{229}Th for Medical Applications: Excitation Functions of Low-Energy Protons on ^{232}Th Targets", Physical Review C, **98**, 044607 (2018).

J. R. Griswold, D. G. Medvedev, J. W. Engle, R. Copping, J. M. Fitzsimmons, V. Radchenko, J. C. Cooley, M. E. Fassbender, D. L. Denton, K. E. Murphy, A. C. Owens, E. R. Birnbaum, K. D. John, F. M. Nortier, D. W. Stracener, L. H. Heilbronn, L. F. Mausner, S. Mirzadeh, "Large Scale Accelerator Production of ^{225}Ac : Effective Cross Sections for 78-192 MeV Protons Incident on ^{232}Th Targets", Applied Radiation and Isotopes, **118**, 366-374, 2016.

S. Hogle, R. A. Boll, K. Murphy, D. Denton, A. Owens, T. J. Haverlock, M. Garland, and S. Mirzadeh, "Reactor Production of Thorium-229", Applied Radiation and Isotopes, **114**, 19-27, 2016.

S. Mirzadeh, Accelerator Produced ^{225}Ac via proton Spallation of ^{232}Th : a joint research program among ORNL, LANL, and BNL, ORNL/TM-2014/142 (2014).

S. Mirzadeh, L.F., Mausner, and M.A. Garland, "Reactor-Produced Medical Radionuclides. In Handbook of Nuclear Chemistry, Second Edition (Volume 4, Radiochemistry and Radiopharmaceutical Chemistry in Life Sciences, Chapter 38, PP 1857 – 1902)", Vertes, A, Nagy, S, Klencsar, Z, Lovas, RG, Roesch, F., editors. New York, NY: Springer (2011)

M. D. Diener, J. M. Alford, S. J. Kennel, and S. Mirzadeh, " $^{212}\text{Pb}@C_{60}$ and its Water-Soluble Derivatives: Synthesis, Stability and Suitability for Radioimmunotherapy", J. Am. Chem. Soc., **129**, 5131, 2007.

Mirzadeh, S., "Generator-produced Alpha-emitters", Proceedings of CIRMS Medical Subcommittee Workshop on Radionuclides Used in Bone Pain Palliation Therapy NIST, Washington D.C., September 27, 1996, *Applied Radiation and Isotopes*, **49**, 345-349 (1998).

R. A. Boll, S. Mirzadeh, and S. J. Kennel, "Optimization of Radiolabeling of Immunoproteins with ^{213}Bi ", Radiochimica Acta **79**, 145-149, (1997).

S. Mirzadeh, K. Kumar and O. A. Gansow, "The Chemical Fate of ^{212}Bi -DOTA Formed by β -Decay of $^{212}\text{Pb}(\text{DOTA})^{2-}$ Complex", *Radiochimica Acta*, **60**, 1-10 (1993).

S. Mirzadeh, M. W. Brechbiel, and O. A. Gansow, "Radiometal Labeling of Immunoproteins: Covalent Linkage of 2-(4-isothiocyanatobenzyl)-DTPA to Immunoglobulin", *Bioconjugate Chemistry* **1**, 59-65 (1990).

Selected Patents:

Mirzadeh, S. and R. M. Lambrecht, "*Methods for the Simultaneous Preparation of Radon-211 and Xe-125, Astatine-211, Iodine-125 and Iodine-123*", U.S. Patent No. 4,644,869, May 12, 1987.

Mirzadeh, S. and R. M. Lambrecht, "*Process for Producing Astatine-211 for Radiopharmaceutical Use*", U.S. Patent No. 4,681,727, July 21, 1987.

Mirzadeh, S., R. E. Whipple, P. M. Grant, H. A. O'Brien, Jr., "*Evaporation-Based Ge/Ga(68) Separation*", U.S. Patent No. 4,268,730, February 3, 1981.

Synergistic Activities:

Organizer of symposiums:

"International Symposium on Targeted Alpha Therapy", June 2013, ORNL

"Radiometals in Therapy and Diagnosis" under auspices of Divisions of Nuclear Chemistry and Technology & Inorganic Chemistry, American Chemical Society National Meeting, Dallas, TX, March 29, 1998.

"Radiochemistry and Radioimmunotherapy", under auspices of Division of Nuclear Chemistry and Technology, American Chemical Society National Meeting, Orlando, FL, August 25-29, 1996.

"Radionuclide Generators for Nuclear Medicine Applications," under auspices of Division of Nuclear Chemistry and Technology, American Chemical Society National Meeting, Washington, D.C., August 23-28, 1992.

Committee Member:

Nuclear Science Advisory Committee (NSAC), Isotopes Subcommittee (2015), The editorial board of the Journal of Applied Radiation and Isotopes (2000-2015). American Chemical Society Divisions of Nuclear Chemistry and Technology (DNCT) and Physical Chemistry, (1979-2010). Review committees for DOE, NIH, and Government of Norway Grant Proposals.

Editorial. Editor of Journal Applied Radiation and Isotopes, 2010 to 2015.

Thesis Advisor and Postgraduate-Scholar Sponsor (Total: 6 Postdoctoral, 8 PhDs; >14 MSc)

Postdoctoral Fellows: Rose Boll, ORNL; Nan Chen, Provision; Ekaterina Dadachova, Univ. of Saskatchewan; Justin Griswold, ORNL; Susan Hogle, ORNL; Jon Woodward, Y-12

PhD Students: Rose Boll, ORNL; Marc Garland, DOE; Justin Griswold, ORNL; Zac Kulage, Pantex; Mark McLaughlin, Univ. of Nebraska Medical; Jessika Rojas, VCU; Miguel Toro-Gonzalez, VCU, Onur Alp Ersöz, Ege University, Turkey.

MSc Students: Jane Wallen, UT, Chelsea Burnham, NuScale Power; D. W. Cagle, FBI; Tyler Cantrell, Cardinal Health; A. M. Craig, UCSD; Justin Griswold, ORNL; James Hinderer, Siemens Medical; Hal Lovett, US Army; Rita Lusk, Norfolk Naval Shipyard; Dairin Malkemus, Univ. of Tennessee; Dan Marsh, Canberra; Jofa Mwakiseg, US Army; Phillip Walsh, LSU; Spencer Walsh, Nuclear Fuel Services, and others

S. Mirzadeh

PUBLICATIONS

Book chapters, reviews, monographs, and proceedings

S. Mirzadeh, Accelerator Produced ^{225}Ac via proton Spallation of ^{232}Th : a joint research program among ORNL, LANL, and BNL, ORNL/TM-2014/142 (2014)

CU Jost, JR Griswold, SH Bruffey, DW Stracener, CL Williams, and S Mirzadeh, “Measurement of cross sections for the $^{232}\text{Th}[p,4n]^{229}\text{Pa}$ reaction at low proton energies”. In proceedings of 22nd International Conference on the Application of Accelerators in Research and Industry, August 5 – 10, 2012, Fort Worth, Texas, USA.

B. J. Egle, S. Mirzadeh, B. A. Tatum, V. K. Varma, E. C. Bradley, T. W. Burgess, W. S. Aaron, J. L. Binder, J. R. Beene, M. Saltmarsh, “A Cyclotron Concept To Support Isotope Production for Science and Medical Applications”, Proceedings of the American Nuclear Society Topical Meeting: Accelerator Applications, Knoxville, TN, April, 2011.

F.F. KNAPP, Jr., S. MIRZADEH, M Garland, B. Ponsard, R. Kuznetsov, 2010, REACTOR PRODUCTION AND PROCESSING OF ^{188}W (Chapter 5). In Production of Long Lived, Parent Radionuclides, for Generators: ^{68}Ge , ^{82}Sr , ^{90}Sr and ^{188}W , IAEA RADIOISOTOPES AND RADIOPHARMACEUTICALS SERIES No. 2.

Mirzadeh, S, Mausner, LF, Garland, MA. “Reactor-Produced Medical Radionuclides. In Handbook of Nuclear Chemistry, Second Edition (Volume 4, Radiochemistry and Radiopharmaceutical Chemistry in Life Sciences, Chapter 38, PP 1857 – 1902)”, Vertes, A, Nagy, S, Klencsar, Z, Lovas, RG, Roesch, F. , editors. New York, NY: Springer (2011).

Garland, MA, Mirzadeh, S, Schenter, RE. 2008. Development of ANS Standard 19.12 Nuclear Data for Isotope Production Calculations for Medical and Other Applications. Trans. American Nuclear Society 98:912.

Lovett, HA, Knight, TW, Garland, MA, Mirzadeh, S. 2007. Evaluation of Tellurium-125 Metastable Production Pathways. Trans. American Nuclear Society 96:363.

Knapp, F. F., Jr., Mirzadeh, S. and Garland, M. “The Availability of Lutetium-177 from Research Reactors, “ pp. 100-109. *Report*, of the 2nd Research Coordination Meeting on the Development of Generator Technologies for Therapeutic Radionuclides, April 3-7, 2006, European Institute of Oncology, Milan, Italy; IAEA, Vienna, Austria.

Knapp, F. F., Jr., Mirzadeh, S., Garland, M. and Ponsard, B. “Reactor Production of Tungsten-188,“ *Invited, for*, IAEA Special Publication, *in preparation*, 2006.

Knapp, F. F., Jr., Mirzaeh, S., and Garland, M. “The Continuing Important Role of High Flux Reactors for Production of Therapeutic Medical Radioisotopes,” *Invited Lecture, For, TECDOC, International Symposium on Trends in Radiopharmaceuticals*, IAEA, Vienna, Austria, *in press*, 2006.

S. Mirzadeh

Book chapters, monographs, and proceedings (cont.)

Boll, R. A., Garland, G., and Mirzadeh, S., "Reactor Production of Thorium-229", Proceedings of the International Conference on Nuclear Data for Science and Technology, Santa Fe, New Mexico, USA, Sept 26, 2004, American Institute of Physics, AIP Conference Proceedings, Haight et al. Editor, Vol. **769**, pp1674-1675 (2005).

Mirzadeh, S., Mausner, L. F., and Garland, M., "Reactor-Produced Medical Radioisotopes", in Handbook of Nuclear and Radiochemistry, A. Vertes, S. Nagy and Z. Klencsar, *Editors*; Kluwer Publishers. Vol. **4**, pp 1-46 (2003).

Mausner, L. F., and Mirzadeh, S., "Reactor Production of Radionuclides in Handbook of Radiopharmaceuticals: Radiochemistry and Applications", M.J. Welch and C. S. Redvanly Editors, John Wiley and Sons Ltd, West Sussex, England, Chapter 3, pp 87-118 (2003).

Du, M., Peretz, F., Boll, R. A., Mirzadeh, S., "Purification of Thorium-229 for Medical Applications", Proceedings of Symposium on Radioanalytical Methods in Interdisciplinary Research, 233rd American Chemical Society National meeting, Orlando, FL, April 10, 2002. ACS Symposium No. 868, C. A. Laue and K. L. Nash Editors, American Chemical Society, WDC, pp 193-203, (2003).

Ponsard, B., Hiltunen, J., Vera-Ruiz, H., Beets, A. L., Mirzadeh, S. and Knapp, F. F., Jr. "The Tungsten-188/Rhenium-188 Generator: Effective Coordination of Tungsten-188 Production Between the HFIR and BR2 Reactors," *J. Radioanalyt. Nucl. Chem.*, **257**, 169-174 (2003).

Knapp, F. F., Jr., Mirzadeh, S., Beets, A. L. and Du, M. "Production of Therapeutic Radioisotopes in the ORNL High Flux Isotope Reactor," *In, Proceedings*, International Isotope Society Meeting, Boston, MA, June 2-6, 2003.

Mirzadeh, S., Du, M. Beets, B., Knapp, Jr. F. F. "Thermo-separation of Neutron Irradiated Tungsten from Re and Os", Proceedings of Nuclear Separations for Radiopharmacy, American Chem. Society, National Meeting, Boston, MA, Aug. 1998, *Industrial and Engineering Chemistry Research*, **39**, 3169-3172 (2000).

Knapp, F. F., Beets, A. L., Mirzadeh, S., Alexander, C. W., and Hobbs, R. L. "Production of Medical Radioisotopes in the ORNL HFIR for Cancer Therapy", Proceedings of the 13th Radiochemical Conference, Marianzke Lazne, Czech Republic, April 19-24, 1998.

Mirzadeh, S., "Generator-produced Alpha-emitters", Proceedings of CIRMS Medical Subcommittee Workshop on Radionuclides Used in Bone Pain Palliation Therapy NIST, Washington D.C., September 27, 1996, *Applied Radiation and Isotopes*, **49**, 345-349 (1998).

Knapp, F. F., Jr., Mirzadeh, S., Beets, A. L., et al., "Reactor-Produced Radioisotopes from ORNL for Bone Pain Palliation", Proceedings of CIRMS Medical Subcommittee Workshop on Radionuclides Used in Bone Pain Palliation Therapy NIST, Washington D. C., September 27, 1996, *Applied Radiation and Isotopes*, **49**, 309-315 (1998).

Boll, R. A., Mirzadeh, S. and Kennel, S. J., "Optimization of Radiolabeling of Immunoproteins with ^{213}Bi ", Proceedings of Symposium on Radiochemistry and Radioimmunotherapy, 212th ACS National Meeting, Orlando, Fl, Aug. 24-28, 1996, *Radiochimica Acta*, **79**, 145-149 (1997).

S. Mirzadeh

Book chapters, monographs, and proceedings (cont.)

Kennel, S. J. and Mirzadeh, S., "Vascular Targeting for Radioimmunotherapy with ^{213}Bi ". Proceedings of Symposium on Radiochemistry and Radioimmunotherapy, 212th ACS National Meeting, Orlando, FL, Aug. 24-28, 1996, *Radiochimica Acta*, **79**, 87-91 (1997).

Boll, R. A., Mirzadeh, S., Kennel, S. J., DePaoli, D. W., and Webb, O. F., "Bi-213 for Alpha-particle-mediated Radioimmunotherapy", Proceedings of XII International Symposium on Radio-pharmaceutical Chemistry, Uppsala, Sweden, June 15-19, 1997, *Journal of Labelled Compounds*, **XL**, 341-343 (1997).

Dadachova, E., Izard, M., and Mirzadeh, S., "Automated Production of Carrier-free Radiolanthanides", Proceedings of XII International Symposium on Radiopharmaceutical Chemistry, Uppsala, Sweden, June 15-19, 1997, *Journal of Labelled Compounds*, **XL**, 254-256 (1997).

Packard, A. B., Spaeth, K., Kronauge, J. F., and Mirzadeh, S., "Platinum-195m Radiopharmaceuticals for Therapy", Proceedings of XII International Symposium on Radiopharmaceutical Chemistry, Uppsala, Sweden, June 15-19, 1997, *Journal of Labelled Compounds*, **XL**, 354-356 (1997).

Mirzadeh, S. and Packard, A. B. (1995), "Synthesis of AZT-Pt(terpy) -- A potential compound for radiotherapy of AIDS", Proceedings of symposium on Advances in Bioconjugate Chemistry, 210th ACS National Meeting, Chicago, Ill, Aug. 20-24, 1995.

Mirzadeh, S. and Knapp, F. F. Jr., "Biomedical Generator Systems", *Journal of Radioanalytical and Nuclear Chemistry - Articles*, **203**, 469-486 (1996).

Mirzadeh, S. and R. M. Lambrecht, "Radiochemistry of Germanium", *Journal of Radioanalytical and Nuclear Chemistry - Articles*, **202**, 7-102 (1996).

Knapp, F. F., Jr. and Mirzadeh, S., "Radionuclide Production, Section 1. Reactors", in *Principles of Nuclear Medicine* (H. N. Wagner, Z. Szabo and J. W. Buchanan, editors), W. B. Sanders, Co., New York, (1995), pp 135-144, ISBN 0-7216-9091-2.

Mahmood, S. T., Mirzadeh, S., Pace, J. V., III, Farrel, K. and Oliver, B. M., *Neutron Dosimetry of the HFIR Hydraulic Tube Facilities*, **ORNL/TM 12831** (1994).

Mirzadeh, S., Alexander, C. W., McManamy, T. and Knapp, F. F., *Projected Medical Radioisotope Production Capabilities of the Advanced Neutron Source (ANS)*, **ORNL/TM-12010S** (1994).

Knapp, Jr., F. F., Mirzadeh, S., Beets, A. L., Sharkey, R., Griffiths, G., and Goldenberg, D. M. "Curie-Scale Tungsten-188/Rhenium-188 Generators Can Cost-Effectively Provide Carrier-Free Rhenium-188 for Routine Clinical Applications," Fourth International Symposium on Technetium and Rhenium in Chemistry and Nuclear Medicine, Bressanone, Italy, September 12-14, 1994, *in press*.

Knapp, Jr., F. F., and Mirzadeh, S. "The Continuing Important Role of Radionuclide Generator Systems for Nuclear Medicine," *Invited Review Article*, European. Journal of Nuclear Medicine, **20**, 1152-1165 (1994).

S. Mirzadeh

Book chapters, monographs, and proceedings (cont.)

Dadachova, E., Mirzadeh, S., Lambrecht, R. M., Hetherington, E. and Knapp, F. F., "Separation of Carrier-free ^{166}Ho from ^{166}Dy in a Biomedical Generator System", in *Synthesis and Applications of Isotopically Labelled Compounds*, John Wiley and Sons Ltd. (1995), pp 229-231.

Dadachova, E., Mirzadeh, S. and Lambrecht, R. M., "Alumina-based $^{188}\text{W}/^{188}\text{Re}$ Biomedical Generator -- Physical and Chemical Study of Tungstate Ion Adsorption on Al_2O_3 ", in *Synthesis and Applications of Isotopically Labelled Compounds*, John Wiley and Sons Ltd. (1995), pp 231-236.

Kamioki, H., Mirzadeh, S., and Lambrecht, "Pre-clinical evaluation of $^{188}\text{W}/^{188}\text{Re}$ Biomedical Generator", 10th International Symposium on Radiopharmaceutical Chemistry, Kyoto, Japan, October 25-28 (1993).

Mirzadeh, S., Di Bartolo, N., Smith, S. V., Lambrecht, R. M., Knapp, F. F. Jr., " $^{166}\text{Dysprosium}-^{166}\text{Holmium}$ *In Vivo* Generator", 10th International Symposium on Radiopharmaceutical Chemistry, Kyoto, Japan, October 25-28 (1993).

Mirzadeh, S., Hetherington, E. and Knapp, F. F., and Lambrecht, R. M., "Carrier-free Holmium-166 from $^{166}\text{Dy}/^{166}\text{Ho}$ Biomedical Generator System, 10th International Symposium on Radiopharmaceutical Chemistry, Kyoto, Japan, October 25-28 (1993).

Mirzadeh, S., "Advances in the $^{188}\text{W}-^{188}\text{Re}$ Generator", in *Proceedings of the International Symposium on Advances in Radiopharmaceuticals*, Sydney, Australia, February 5, 1993.

Mirzadeh, S., R. E. Schenter, A. P. Callahan and F. F. Knapp, *Production Capabilities in U. S. Nuclear Reactors for Medical Radioisotopes*, **ORNL/TM-12010** (1992).

Mirzadeh, S., D. E. Rice, A. P. Callahan and F. F. Knapp, Jr., "The $^{194}\text{Os}/^{194}\text{Ir}$ Generator -- Production and Purification of ^{194}Os ", in *Proceedings of the IX International Symposium on Radiopharmaceutical Chemistry*, Paris, France, April 6-10 (1992), pp 471-473.

Brechbiel, M. W., C. G. Pippin, S. Mirzadeh, C. Wu, T. J. McMurry, O. A. Gansow, D. Colcher, D. E. Milenic, M. Roseli, R. Huneke and M. Strand, "Synthesis of 2-(p-SCN-benzyl)- trans-cyclohexyl-DTPA for α -particle Mediated Radioimmunotherapy", in *Proceedings of the IX International Symposium on Radiopharmaceutical Chemistry*, Paris, France, April 6-10 (1992), pp375-378.

Knapp, F. F. Jr., E. C. Lisic, S. Mirzadeh, A. P. Callahan, and D. E. Rice, "A New Clinical Prototype Tungsten-188/Rhenium-188 Generator to Provide High Levels of Carrier-free Rhenium-188 for Radioimmunotherapy (RIT)", in *Proceedings of the European Association of Nuclear Medicine Meeting*, Vienna, Austria, September 1-5, 1991; Nuclear Medicine in Research and Practice, Schattauer Verlag, Stuttgart, pp 183-186 (1992).

Mirzadeh, S. and Y. Y., Chu "Production of Ga-66, A Positron Emitter for Radioimmunotherapy", in *Proceedings of the International Conference on Nuclear Data for Science and Technology*, Julich, Germany, May 1991, S. M. Qaim Editor, (ISBN 0-387-55100X), Springer Verlag, New York (1992) pp 619-621.

S. Mirzadeh

Book chapters, monographs, and proceedings (cont.)

Mirzadeh, S., F. F. Knapp, Jr. and A. P. Callahan, "Production of Tungsten-188 and Osmium-194 in a Nuclear Reactor for New Clinical Generators". In *Proceedings of the International Conference on Nuclear Data for Science and Technology*, Julich, Germany, May 1991, S. M. Qaim Editor, (ISBN 0-387-55100X), Springer Verlag, New York (1992) 595-597.

Knapp, F. F. Jr., A. P. Callahan, S. Mirzadeh, C. Brihaye and M. Guillaume, "The Development of New Radionuclide Generator Systems for Nuclear Medicine Applications", in *Progress in Radiopharmacy* (P. A. Schubiger and G. Westera eds.), Development in Nuclear Medicine Series, Vol. 22 (ISBN 0-387-55100-x), Kluwer Academic Publishers (1992) pp 67-88.

Gansow, O. A., M. W. Brechbiel, S. Mirzadeh, D. Colcher and M. Roselli, "Chelates and Antibodies: Current Methods and New Directions". In *Cancer Imaging with Radiolabeled Antibodies*, D. M. Goldenberg editor, Kluwer Academic Publishers (1990) pp 153-171.

Pippin, C. G., S. Mirzadeh, and O. A. Gansow, "Kinetics of the Isotope Exchange Between Copper(II) and Copper(II)-1,4,7-Triazacyclonane-N,N',N'' Triacetate". In *Proceedings of the 5th International Symposium on Radiopharmaceutical Chemistry*, Princeton, New Jersey, June 1990, Journal of Labeled Compounds and Radiopharmaceuticals, **29** (suppl.), 227-229 (1990).

Clem, R., R. M. Lambrecht, S. Mirzadeh, C. G. Pippin, M. W. Brechbiel, M. Roselli, O. A. Gansow, and D. Colcher, "Radiochemistry of Lead-203 for Radiolabeling Antibody Conjugates". *Proceedings of the 5th International Symposium on Radiopharmaceutical Chemistry*, Princeton, New Jersey, June 1990, Journal of Labeled Compounds and Radiopharmaceuticals, **29** (suppl.), 335-337 (1990).

Mirzadeh, S. and R. M. Lambrecht, "Measurement of the Cyclotron Beam Energy of the Alpha Particle by Rutherford Scattering in Gold Foil". In *Proceedings of the IAEA Consultants' meeting on Data Requirements for Medical Radioisotope Production*, K. Okamoto Editor, IAEA INDC(NDC)-195/GZ January 1988.

Mausner, L. F., R. Mahr, J.A. Vachiere S. C. Srivastava and S. Mirzadeh, "Production of High Specific Activity Sn-117m the Szilard-Chalmers Process". In *Proceedings of the 7th International Symposium on Radiopharmaceutical Chemistry, Groningen, the Netherlands*, July 1988, Journal of Labeled Compounds and Radiopharmaceuticals, **26** (suppl.), 177-178 (1988).

Gansow, O. A., M. W. Brechbiel, S. Mirzadeh, M. Roselli, D. Colcher, A. Raubitschek and J. Schlom. "Difference in the Biodistribution of Indium and Yttrium Labeled Monoclonal Antibodies". In *Proceedings of the 7th International Symposium on Radiopharmaceutical Chemistry, Groningen, the Netherlands*, July 1988, Journal of Labeled Compounds and Radiopharmaceuticals, **26** (suppl.), 290-292 (1988).

Mausner, L. F., S. Mirzadeh, and S. C. Srivastava, "A New Spallation Radionuclide Research and Production Facility". In *Proceedings of the 6th International Symposium on Radiopharmaceutical Chemistry*, Boston, Massachusetts, June 1986, Journal of Labeled Compounds and Radiopharmaceuticals, **18** (suppl.), 1280-1283 (1986).

S. Mirzadeh

Book chapters, monographs, and proceedings (cont.)

Mirzadeh, S., L. F. Mausner, and S. C. Srivastava, "Design of a Fully Automated, In-Beam, Continuous-Flow I-123 Production System". In *Proceedings of the 6th International Symposium on Radiopharmaceutical Chemistry*, Boston, Massachusetts, June 1986, *Journal of Labeled Compounds and Radiopharmaceuticals*, **18** (suppl.), 1386-1388 (1986).

Mausner, L. F., S. Mirzadeh, T. Prach, and P. Richards, "Production and Separation of Tin-117m for Bone Radiotherapy". In *Proceedings of the 5th International Symposium on Radiopharmaceutical Chemistry*, Tokyo, Japan, July 1984, *Journal of Labeled Compounds and Radiopharmaceuticals*, **11** (suppl.), 1284-1285 (1984).

Mirzadeh, S., M. Kahn, P. Grant, and H. A. O'Brien, Jr., "A Distillation-based Ge(68)-Ga(68) Positron Generator". In *Proceedings of the Second International Congress of the World Federation of Nuclear Medicine and Biology*, Washington, D.C., 1978.

S. Mirzadeh

Publications in referred journals

A. C. Peacock, R. Copping, J. R. Griswold, R. A. Boll, D. L. Denton, J. A. Gaugler, Widner, K. E. Murphy, D. Stracener. and S. Mirzadeh, "Separation of Radium from Barium and other Group II Elements Using Reverse Phase Cation Exchange Chromatography in Citrate Media" for submission to *Radiochimica Acta* (2022) (under internal review).

J. G. Mwakisege, G. Schweitzer and S. Mirzadeh, "Synthesis and Stability of Actinium-225 Endohedral Fullerenes, $^{225}\text{Ac}@C_{60}$ ", *ACS Omega* 5(42):27016-27025, October 2020, DOI:10.1021/acsomega.0c01659.

S. Mirzadeh, "Innovation, Impact and Strategic Importance of Alpha Emitting Radionuclides", *Journal of Medical Imaging and Radiation Sciences*, **50**, S6-S10 (2019).

L. Królicki, F. Bruchertseifer, J. Kunikowska, H. Koziara, B. Królicki, M. Jakuciński, D. Pawlak, C. Apostolidis, S. Mirzadeh, R. Rola, A. Merlo, A. Morgenstern, "Safety and efficacy of targeted alpha therapy with ^{213}Bi -DOTA-substance P in recurrent glioblastoma", *European Journal of Nuclear Medicine and Molecular Imaging*, 46(3):614-622 (2019).

Kathleen Broderick, Rita Lusk, James Hinderer, Justin Griswold¹, Rose Boll, Marc Garland, Lawrence Heilbronn, and Saed Mirzadeh, "Reactor Production of Promethium-147", *Applied Radiation and Isotopes*, **144**, 54-63 (2018)

M. Toro González, D. M. Clifford, R. Copping, S. Mirzadeh, J. V. Rojas, "Synthesis and Characterization of Intrinsically Radiolabeled Lanthanide Phosphate Nanoparticles Toward Biomedical and Environmental Applications", *J. Nanoparticle Research*, **20** (238), article id. 238, 15 pp (2018).

M. Toro González, R. Copping, S. Mirzadeh, J. V. Rojas, "Multifunctional GdVO_4 : Eu Core-Shell Nanoparticles containing ^{225}Ac for Targeted Alpha Therapy and Molecular Imaging. *J. Materials Chemistry B*, 6, 7985- 7997 (2018)

Jonathan M. Fitzsimmons, Bryna Torre, Bryan James Foley, Roy Copping, David E. Hill, Saed Mirzadeh, Cathy S. Cutler, Leonard Mausner, and Dmitri Medvedev, "Evaluation of SynPhase Lanterns for capturing Ac-225 from bulk thorium", *Journal of Radioanalytical and Nuclear Chemistry*, 318 (1), 477-483 (2018).

L. Krolicki, F. Bruchertseifer, J. Kunikowska, H. Koziara, B. Królicki, M. Jakuciński, D. Pawlak, C. Apostolidis, S. Mirzadeh, R. Rola, A. Merlo, A. Morgenstern, Prolonged survival in secondary glioblastoma following local injection of targeted alpha therapy with ^{213}Bi -substance P analogue, *European Journal of Nuclear Medicine and Molecular Imaging*, **45**(9), 1636-1636 (2018)

Justin R. Griswold, Cara U. Jost, Daniel W. Stracener, Stephanie H. Bruffey, David Denton, Marc Garland, Lawrence Heilbronn, and Saed Mirzadeh, "Production of ^{229}Th for Medical Applications: Excitation Functions of Low-Energy Protons on ^{232}Th Targets", *Physical Review C* **98**, 044607 (2018).

Publications in referred journals

Michael E. Autenrieth, Christof Seidl, Frank Bruchertseifer, Thomas Horn, Florian Kurtz, Benedikt Feurecker, Calogero D'Alessandria, Christian Pfob, Christos Apostolidis, Jürgen E. Gschwend, Markus Schwaiger, Klemens Scheidhauer, Saed Mirzadeh and Alfred Morgenstern, "Treatment of carcinoma *in situ* of the urinary bladder with an alpha-emitter immunoconjugate targeting the epidermal growth factor receptor: A pilot study", *European Journal of Nuclear Medicine and Molecular Imaging*, **45**(8):1364-1371 (2018)

Li, M., Zhang, X.; Quinn, T. P., Lee, D., Liu, D., Kunkel, F.; Zimmerman, B. E., McAlister, D., Olewein, K., Menda, Y., Mirzadeh, S., Copping, R., Johnson, F. L., Schultz, M. K., Automated cassette-based production of high specific activity [$^{203}\text{Tl}/^{212}\text{Pb}$]peptide-based theragnostic radiopharmaceuticals for image-guided radionuclide therapy for cancer. *Applied Radiation and Isotopes*, **127**, 52-60 (2017).

Radchenko, V., Mastren, T., Meyer, C. A. L., Ivanov, A. S., Bryantsev, V. S., Copping, R., Denton, D., Engle, J. W., Griswold, J. R., Murphy, K., Wilson, J. J., Owens, A.; Wyant, L.; Birnbaum, E. R.; Fitzsimmons, J.; Medvedev, D.; Cutler, C. S.; Mausner, L. F., Nortier, M. F., John, K. D., Mirzadeh, S., Fassbender, M. E., Radiometric evaluation of diglycolamide resins for the chromatographic separation of actinium from fission product lanthanides. *Talanta*, **175**, 318-324 (2017)

Jelenska, J., Davern, S., Standaert, R., Mirzadeh, S., Greenberg, J-T., "Flagellin peptide flg22 gains access to long-distance trafficking in Arabidopsis via its receptor, FLS2" *Journal of Experimental Botany*, Vol. **68**, 1769 (2017).

J. R. Griswold, D. G. Medvedev, J. W. Engle, R. Copping, J. M. Fitzsimmons, V. Radchenko, J. C. Cooley, M. E. Fassbender, D. L. Denton, K. E. Murphy, A. C. Owens, E. R. Birnbaum, K. D. John, F. M. Nortier, D. W. Stracener, L. H. Heilbronn, L. F. Mausner, S. Mirzadeh, "Large Scale Accelerator Production of ^{225}Ac : Effective Cross Sections for 78-192 MeV Protons Incident on ^{232}Th Targets", *Applied Radiation and Isotopes*, **118**, 366-374 2016.

Susan Hogle, Rose Ann Boll, Karen Murphy, David Denton, Allison Owens, Tamara J. Haverlock, Marc Garland, and Saed Mirzadeh, "Reactor Production of Thorium-229", *Applied Radiation and Isotopes*, **114**, 19-27, 2016.

Sandra M. Davern, Timothy E. McKnight, Robert F. Standaert, Jennifer L. Morrell-Falvey, Elena D. Shpak, Udaya C. Kalluri, Joanna Jelenska, Jean T. Greenberg and Saed Mirzadeh, "Carbon Nanofiber Arrays: A Novel Tool for Microdelivery of Biomolecules to Plants", *PLoS ONE*, DOI:10.1371/journal.pone.0153621, pp1-26, April 27, 2016.

Justin Jeet, Christian Schneider, Scott T. Sullivan, Wade G. Rellergert, Saed Mirzadeh, A. Cassanho, H. P. Jenssen, Eugene V. Tkalya, and Eric R. Hudson, "Results of a direct search using synchrotron radiation for the low-energy ^{229}Th nuclear isomeric transition", *Phys. Rev. Lett.*, **114**, 253001(1-6) (2015).

Jessika V. Rojas, Jonathan Woodward, Nan Chen, Adam J. Rondinone, Carlos H. Castano, and Saed Mirzadeh, (2015) "Synthesis and characterization of lanthanum phosphate nanoparticles as carriers for ^{223}Ra and ^{225}Ra for targeted alpha therapy", *J. Nucl. Med. Biology*, **42**, 614-620 (2015).

S. Mirzadeh

Publications in referred journals

Mark F. McLaughlin, David Robertson, Paul H. Pevsner, Jonathan S. Wall, Saed Mirzadeh, and Stephen J. Kennel, "LnPO₄ nanoparticles doped with Ac-225 and sequestered daughters for targeted alpha therapy", *Cancer Biotherapy and Radiopharmaceuticals*, **29**(1), 34-41, (2014).

Mark F. McLaughlin, Jonathan Woodward, Rose A. Boll, Adam J. Rondinone, Saed Mirzadeh, and J. David Robertson, "Gold-Coated Lanthanide Phosphate Nanoparticles for an ²²⁵Ac in vivo Alpha Generator", *Radiochimica Acta*, **101**, 595-600, (2013).

Delmau L. L., Moine J.M., Mirzadeh S., and Moyer B. A. (2013) "First Experimentally Determined Thermodynamic Values of Francium: Hydration Energy, Energy of Partitioning, and Thermodynamic Radius", *J. Physical Chemistry B*, **117**(31), 9258-9261.

McLaughlin M. F., Woodward J., Boll R.A., Wall J. S., Rondinone A. J., Kennel S. J., Mirzadeh S., and Robertson J.D., "Gold Coated Lanthanide Phosphate Nanoparticles for Targeted Alpha Generator Radiotherapy" *PLOS One*, 8/1, e54531 (2013).

Woodward J., Kennel S.J., Stuckey A., Osborne D., Wall J., Rondinone A., Standaert R.F., and Mirzadeh S., 2011, "LaPO₄ Nanoparticles Doped with Actinium-225 that Partially Sequester Daughter Radionuclides", *Bioconjugate Chemistry*, **22**, 766-776 (2011).

Kennel, S. J., Woodward, J. D., Rondinone, A. J., Wall, J., Huang, Y, Mirzadeh, S., "The Fate of MAb targeted Cd^{125m}Te/ZnS nanoparticles *in vivo*", *J. Nucl. Med. Biology*, **35**, Issue 4, May 2008, Pages 501-514

Diener, M. D., Alford, J. M., Kennel, S. J., Mirzadeh, S., "²¹²Pb@C₆₀ and its Water-Soluble Derivatives: Synthesis, Stability and Suitability for Radioimmunotherapy", *J. Am. Chem. Soc.*, **129**, 5131 (2007).

Diener, M. D., Alford, J. M., Williamson, K. A., Mirzadeh, S. "¹⁷⁷Lu @C₆₀ and its Water-Soluble Derivatives: Production, Purification and Potential for Radioimmunotherapy", *Chem. Phys. Lett* (2007). (submitted).

Woodward, J. D., Kennel, S. J., Mirzadeh, S., Dai, S., Wall, J., Richey T., Avenell, J., Rondinone, A. J., "In vivo SPECT/CT imaging and biodistribution using radioactive Cd^{125m}Te/ZnS nanoparticle", *Nanotechnology* **18**, 175103 - 175108 (2007).

Kennel, S., Lankford, T., Garland, M, Sundberg, J., P., Mirzadeh, S., "Biodistribution of ²²⁵Ra citrate in mice: retention of daughter radioisotopes in bone", *Nuclear Medicine and Biology*, **32**, 859-867 (2005).

Boll, R. A., Malkemus, D., and Mirzadeh, S. "Production of Actinium-225 for Alpha Particle Mediated Radioimmunotherapy". *Applied Radiation and Isotopes*, **62**, pp 667-679 (2005).

Haverlock, T. J., Mirzadeh, S., and Moyer, B. A., "Selectivity of Calix [4] arene-bis(benzocrown-6) in the Complexation and Transport of Francium Ions", *Journal of American Chemical Society*, **125**, 1126-1127 (2003).

Garland, M. A., Mirzadeh, S., Alexander, C. W., Hirtz, G. J., Hobbs, R. W., and Knapp, F. F. Jr., "Flux Characterization of a Peripheral Target Position in the High Flux Isotope Reactor", *Applied Radiation and Isotopes*, **59**, 63-72 (2003).

Publications in referred journals

Mirzadeh, S., Lambrecht, F. Y., Lambrecht, R. M., "Decay of Tungsten-189", *Applied Radiation and Isotopes B Richard Lambrecht Memorial Issue*, **56**, 637-640 (2002).

Kennel, S. J., Mirzadeh, S., Eckelman, W. C., Waldmann, T. A., Garmastani, K., Yordanov, A. T., Stabin, M., and Brechbiel, M. W., "Vascular Targeted Radioimmunotherapy with the α -emitter ^{211}At ", *Radiation Research*, **157**, 633-641 (2002).

Kennel, S. J., Brechbiel, M. W., Milenic, D. E., Schlom, J., and Mirzadeh, S. "Actinium-225 Conjugates of Mab CC49 and Humanized DCH2CC49: Therapy of LS174T Tumors in Nude Mice", *Cancer Biotherapy and Radiopharmaceuticals*, **17**, 219-231 (2002).

Kennel, S. J., Lankford, T. K., Davern, S., Foote, L., Taniguchi, K., Ohizumi, I., Tsutsumi, Y., Nakagawa, S., Mayumi, T., and Mirzadeh, S., "A Therapy of Rat Tracheal Carcinoma IC-12 in SCID Mice: Vascular Targeting with Bi-213-MAb TES-23", *European Journal of Cancer*, **38**, 1278-1287 (2002).

Milenic, D. E., Roselli, M., Mirzadeh, S., Pippin, G. C., Gansow, O. A., Cocher, D., Brechbiel, M. W., and Schlom, J. "In Vivo Evaluation of Bismuth-Labeled Monoclonal Antibody Comparing DTPA-Derived Bifunctional Chelates", *Cancer Biotherapy and Radiopharmaceuticals*, **16**, 133-146 (2001).

Mirzadeh, S., Du, M., Beets, A., Knapp, F. F. Jr., "Thermo-separation of Neutron Irradiated Tungsten from Re and Os", *Industrial and Engineering Chemistry Research*, **39**, 3169-3172 (2000).

Kennel, S. J., Chappell, L. L., Dadachova, K., Brechbiel, M. W., Lankford, T. K., Davis, I. A., Stabin, M., and Mirzadeh, S., "Evaluation of ^{225}Ac for Vascular Targeted Radioimmunotherapy of Lung Tumors", *Cancer Biotherapy and Radiopharmaceuticals*, **15**, 235-244 (2000).

Kennel, S. J., Mirzadeh, S., Hurst, G. B., Foote, L. J., Lankford, T. K., Glowienka, K. A., Chappell, L. L., Kelso, J. R., Davern, S. M., Safavy, A., Brechbiel, M. W., "Labeling and Distribution of Linear Peptides Identified Using in-vivo Phage Display Selection for Tumors", *Journal of Nuclear Medicine and Biology*, **27**, 815-825 (2000).

Cagle, D. W., Kennel, S. J., Mirzadeh, S., Alford, M. J., Wilson L. J., "In vivo Studies of Fullerene-based Materials Using Endohedral Metallofullerene Radiotracer" *Proceedings of National Academy of Sciences*, **96**, 5182-5187 (1999).

Wilson, L. J., Cagle, D. W., Thrash, T. P., Kennel, S. J., Mirzadeh, S., Alford, M. J., Ehrhardt, G. J., "Metallofullerene Drug Design", *Coordination Chemistry Reviews*, **190**, 199 (1999)

Thrash, T. P., Cagle D. W., Alford, J. M., Wright, K., Ehrhardt, G. J., Mirzadeh, S., Wilson L. J., "Toward Fullerene-Based Radiopharmaceuticals: High Yield Neutron Activation of Endohedral ^{165}Ho Metallofullerenes", *Chemical Physics Letter*, 12673 (1999).

Kennel, S. J., Lankford, P. K., Foote, L. J., Davis, I. A., Boll, R. A., and Mirzadeh, S., "Combination Vascular Targeted and Tumor Targeted Radioimmunotherapy", *Cancer Biotherapy and Radiopharmaceuticals*, **14**, 371-379 (1999).

S. Mirzadeh

Publications in referred journals

Deal, K. A., Davis, I. A., Mirzadeh, S., Kennel, S. J., Brechbiel, M. W. "Improved *In Vivo* Stability of Actinium-225 Complexes", *Journal of Medicinal Chemistry*, **42**, 2988-2992 (1999).

Davis, I. A., Glowienka, K. A., Boll, R. A., Deal, R. A., Brechbiel, M. W., Stabin, M., Bochsler, P. N., Mirzadeh, S., Kennel, S. J., "Comparison of Actinium-225 Chelates: Tissue Distribution and Radiotoxicity", *Journal of Nuclear Medicine and Biology*, **26**, 581-589 (1999).

Kennel, S. J., Boll, R., Stabin, M., Schuller, H. M. and Mirzadeh, S., "Radioimmunotherapy of Micrometastases in Lung with Vascular Targeted ^{213}Bi ", *British Journal of Cancer* **80**, 175-184 (1999).

Kennel, S. J., Stabin, M., Foote, L. J., Lankford, P. K., Terzaghi-Howe, M., Patterson, H., Barkenbus, J., Popp, D. M. and Mirzadeh, S., "Toxicity and Microdosimetry for ^{213}Bi Bound to Membranes of Monolayer and Spheroid Cultures of Tumor Cells", *Radiation Research*, **151**, 244-256 (1999).

Kennel, S. J., Stabin, M., Yoriyaz, H., Brechbiel, M., and Mirzadeh, S., "Treatment of Lung Tumor Colonies with ^{90}Y Targeted to Blood Vessel - Comparison with the α -particle Emitter ^{213}Bi ", *Journal of Nuclear Medicine and Biology*, **26**, 149-157 (1999).

Roselli, M., D. E. Milenic, S. Mirzadeh, M. Brechbiel, C. G. Pippin, O. A. Gansow, D. Colcher, and J. Schlom. "Biodistribution Studies of Indium-111 and Yttrium-Labeled MAB B72.3 using DTPA-derived Bifunctional Chelates ", *Journal of International Society of Tumor Targeting*. **1**, 20-40 (1999).

Roselli, M., D. E. Milenic, M. Brechbiel, S. Mirzadeh, C. G. Pippin, O. A. Gansow, D. Colcher, and J. Schlom, "In Vivo Comparison of CHX-DTPA Ligand Isomers in Athymic Mice Bearing Carcinoma Xenografts", *Cancer Biotherapy and Radiopharmaceuticals* **14**(3):209-20, 1999.

McMurry, T. J., Pippin, G. C., Wu, C., Kim, D. A., Brechbiel, M. W., Mirzadeh, S., and Gansow, O. A., "Physical Parameters and Biological Stability of Yttrium (III) Diethylenetriaminepentaacetic Acid Derivative Conjugates" *Journal of Medicinal Chemistry*, **41**, 3546-3549 (1998).

Kennel, S. J. and Mirzadeh, S., "Vascular Targeting for Radioimmunotherapy with ^{213}Bi -- an Alpha Particle Emitter", *Journal of Nuclear Medicine and Biology*, **25**, 241-246 (1998).

Wang, S. J., Lin, W. Y., Chen, M. N., Hsieh, B. T., Mirzadeh, S., Knapp, F. F. , Jr., "Rhenium-188 Microspheres: A new Radiation Synovectomy Agent", *Nuclear Medicine Communications*, **19**, 427-433 (1998).

Wang, S. J., Lin, W. Y., Chen, M. N., Hsieh, B. T., Mirzadeh, S., Knapp, F. F., Jr., "Intratumoral Injection of Rhenium-188 Microspheres into an Animal Model of Hepatoma", *Journal of Nuclear Medicine*, **39**, 1752-1757 (1998).

Boll, R. A., Mirzadeh, S. and Kennel, S. J. (1997), "Optimization of Radiolabeling of Immunoproteins with ^{213}Bi ", *Radiochimica Acta* **79**, 145-149.

Mirzadeh, S. and Walsh, P., "Numerical Evaluation of the Production of Radionuclides in a Nuclear Reactor -- Part I", *Applied Radiation and Isotopes*, **49**, 379-382 (1997).

S. Mirzadeh

Publications in referred journals

- Mirzadeh, S. and Walsh, P., "Numerical Evaluation of the Production of Radionuclides in a Nuclear Reactor -- Part II", *Applied Radiation and Isotopes*, **49**, 383-395 (1997).
- Mirzadeh, S., Knapp, F. F., Jr. and Lambrecht, R. M., "Burn-up cross-section of W-188", *Radiochimica Acta*, **77**, 99-102 (1997).
- Dadachova, E. and Mirzadeh, S., "The Role of Tin in Direct Labeling of Proteins with Rhenium-188", *J. Nuclear Medicine and Biology*, **6**, 605-608 (1997).
- Mirzadeh, S., C. W. Alexander and F. F. Knapp, Jr., "Evaluation of Neutron Inelastic Scattering, [n,n'], for Production of High Spin ^{117m}Sn , ^{119m}Sn and ^{195m}Pt Isotopes", *Applied Radiation and Isotopes*, **48**, 441-446 (1997).
- Dadachova, E., Mirzadeh, S., Smith, S. V., Knapp, F. F. Jr. and Hetherington, E. L. "Radiolabeling Antibodies with Holmium-166", *Applied Radiation and Isotopes* **48**, 477-481 (1997).
- Dadachova, E., Mirzadeh, S. and Lambrecht, R. M., "Tungstate-Ion-Alumina Interaction in a $^{188}\text{W}/^{188}\text{Re}$ Biomedical Generator", *Journal of Physical Chemistry* **99**, 10976-10981 (1995).
- Smith, S. V., Di Bartolo, N, Mirzadeh, S., Lambrecht, R. M. and Knapp, F. F. Jr., "[^{166}Dy] Dysprosium/[^{166}Ho] Holmium *In Vivo* Generator", *Applied Radiation and Isotopes* **46**, 759-764 (1995).
- Dadachova, E., Mirzadeh, S., Lambrecht, R. M., Hetherington, E. and Knapp, F. F., "Separation of Carrier-free ^{166}Ho from Dy_2O_3 Targets by Partition Chromatography and Electrophoresis", *Journal of Radioanalytical and Nuclear Chemistry - Letters*, **199**, 115 (1995).
- Dadachova, E., Mirzadeh, S., Lambrecht, R. M., Hetherington, E. and Knapp, F. F., "Separation of Carrier-free Holmium-166 from Neutron-irradiated Dysprosium Targets", *Journal of Analytical Chemistry*, **66**, 4272-4277 (1994).
- Knapp, F. F., Jr., Callahan, A. P., Beets, A. L., Mirzadeh, S., and Hsieh. B.-T. "Processing of Reactor-Produced Tungsten-188 for Fabrication of Clinical Scale Alumina-Based Tungsten-188/Rhenium-188 Generators" *Applied Radiation and Isotopes*, **45**, 1123-1128 (1994).
- Kamioki, H., Mirzadeh, S., Lambrecht, R. M., Knapp, F. F. and Dadachova, E., " $^{188}\text{W}/^{188}\text{Re}$ Generator for Biomedical Applications", *Radiochimica Acta*, **65**, 39-46 (1994).
- Junghans, R. P., Dobbs, D., Raubitschek, A. A., Brechbiel, M. W., Mirzadeh, S., Gansow, O. A. and Waldmann, T. A., "Pharmacokinetics and Bioactivity of DOTA-Bismuth Conjugated Anti-Tac Antibody for Alpha Emitter Therapy", *Cancer Research*, **53**, 5683-9 (1993).
- Mirzadeh, S., K. Kumar and O. A. Gansow, "The Chemical Fate of ^{212}Bi -DOTA Formed by β -Decay of $^{212}\text{Pb}(\text{DOTA})^{2-}$ Complex", *Radiochimica Acta*, **60**, 1-10 (1993).

S. Mirzadeh

Publications in referred journals

- Lisic, E. C., S. Mirzadeh, F. F. Knapp, Jr., "Synthesis of Carrier-free Rhenium-188(V)DMSA Using Triphenyl Phosphine as a Facile Reducing Agent", *Journal of Labeled Compounds and Radiopharmaceuticals* **XXXIII**, 65-76 (1993).
- Mirzadeh, S. and F. F. Knapp, Jr., "Spontaneous Electrochemical Separation of Carrier-free ^{64}Cu and ^{67}Cu from Zn Targets", *Radiochimica Acta*, **57**, 193-199 (1992).
- Mausner, L. F., S. Mirzadeh, and S. C. Srivastava "Improved Specific Activity of $^{117\text{m}}\text{Sn}$ with the Szilard-Chalmers Process", *Applied Radiation and Isotopes* **43**, 1117-1122 (1992).
- Mirzadeh, S., D. E. Rice and F. F. Knapp, Jr., "Carrier-free ^{194}Ir from an $^{194}\text{Os}/^{194}\text{Ir}$ Generator - A New Candidate for Radioimmunotherapy", *Applied Radiation and Isotopes* **43**, 689-692(1992).
- Roselli, M., J. Schlom, O. A. Gansow, M. Brechbiel, S. Mirzadeh, C. G. Pippin, D. E. Milenic and D. Colcher. "Comparative Biodistribution Studies of DTPA-derivative Bifunctional Chelates for Radiometal Labeled Monoclonal Antibodies", *Nuclear Medicine and Biology* **18**, 389-394 (1991).
- Brechbiel, M, S. Mirzadeh, O. A. Gansow, "Backbone-substituted DTPA-Ligands for Radioimmunotherapy with Yttrium-90", *Bioconjugate Chemistry* **2**, 187-189 (1991).
- Coursey B. M., J. M. Calhoun, J. Cessna, D. D. Hoppe, A. P. Callahan, S. Mirzadeh, and F. F. Knapp, Jr., "Assay of the Eluent from the Alumina-Based Tungsten-188/Rhenium-188 Generator", *Journal of Radiochemistry and Radioisotopes* **1**, No. 4, 38-49 (1990).
- Mirzadeh, S., M. W. Brechbiel, and O. A. Gansow, "Radiometal Labeling of Immunoproteins: Covalent Linkage of 2-(4-isothiocyanatobenzyl)-DTPA to Immunoglobulin", *Bioconjugate Chemistry* **1**, 59-65 (1990).
- Cooper, M. M., R. C. Roberts, C. K. Goldman, S. Mirzadeh, C. Stone, O. A. Gansow, R. E. Clark and T. A. Waldmann, "Use of Yttrium-90-labeled Anti-Tac Antibody in Primate Xenograft Transplantation", *Journal of Transplantation* **50**, 760-765 (1990).
- Ruegg, C. L., W. T. Anderson-Berg, M. W. Brechbiel, S. Mirzadeh, O. A. Gansow and M. Strand, "Improved *in vivo* Stability and Tumor Targeting of Bismuth-Labeled Antibody", *Cancer Research* **50**, 4221-4226 (1990).
- Mausner, L. F., S. Mirzadeh, H. Schnakenberg and S. C. Srivastava, "The Design and Operation of the Upgraded BLIP Facility for Radionuclide Research and Production", *Applied Radiation and Isotopes* **41**, 367-374 (1990).
- Kozak, R. W., A. Raubitschek, S. Mirzadeh, M. W. Brechbiel, R. Junghans, O. A. Gansow, and T. A. Waldmann, "The Nature of the Bifunctional Chelating Agent Used for Radioimmunotherapy with Yttrium-90 Monoclonal Antibodies as a Critical Factor in Determining *In Vivo* Survival and Organ Toxicity", *Cancer Research*, **49**, 2639-2644 (1989).

S. Mirzadeh

Publications in referred journals

Roselli, M., J. Schlom, O. A. Gansow, A. Raubitschek, S. Mirzadeh, M. Brechbiel and D. Colcher. "Comparative Biodistribution of Yttrium and Indium Labeled Monoclonal Antibody B72.3 in Athymic Mice Bearing Human Colon Carcinoma Xenografts", *Journal of Nuclear Medicine*, **30**, 672-682 (1989).

Mirzadeh, S. and M. Kahn, "Studies of the Chemical Behavior of Carrier-free Ge-68: III. Adsorptive Properties", *Radiochimica Acta*, **39**, 189 (1986).

Mirzadeh, S., Y. Y. Chu, S. Katcoff, and L. K. Peker, "Decay of 7.1-min Th-235", *Journal of Physical Review C*, **33**, 2159 (1986).

Mirzadeh, S. and M. Kahn, "Studies of the Chemical Behavior of Carrier-free Ge-68: II. A Determination of the Distribution Constant from the Distillation of the Azeotropic HCl", *Radiochimica Acta*, **39**, 73 (1986).

Mausner, L. F., S. C. Srivastava, S. Mirzadeh, G. E. Meinken, and T. Prach, "I-123 Research and Production at Brookhaven", *International Journal of Applied Radiation and Isotopes*, **37**, 843 (1986).

Mausner, L. F., S. Mirzadeh, and T. E. Ward, "Nuclear Data for Production of Sn-117m for Biomedical Applications", *Journal of Radiation Effects*, **94**, 59 (1986).

Mirzadeh, S., L. F. Mausner, and S. C. Srivastava, "Production of No-carrier-added Cu-67", *International Journal of Applied Radiation and Isotopes*, **37**, 29, (1986).

Lambrecht, R. M. and S. Mirzadeh, "Cyclotron Isotopes and Radiopharmaceuticals, XXXV. Astatine-211", *International Journal of Applied Radiation and Isotopes*, **36**, 443 (1985).

Lambrecht, R. M. and S. Mirzadeh, "Astatine-211: Production, Radiochemistry and Nuclear Data", *Journal of Labeled Compounds and Radiopharmaceuticals*, **11**, 1288-1289 (1984).

Bloomer, W. D., W. H. McLaughlin, R. M. Lambrecht, R. W. Atcher, S. Mirzadeh, J. L. Madara, R. A. Milius, M. R. Zalutsky, S. J. Adelstein, and A. P. Wolf, "At-211 Radiocolloid Therapy: Further Observations and Comparisons with Radiocolloids of P-32, Dy-165, and Y-90", *International Journal of Radiation Oncology and Biological Physics*, **10**, 341 (1984).

Mirzadeh, S., Y. Y. Chu, S. Katcoff, and L. K. Peker, "Decay of 37.5-min Th-236 and 9.1-min Pa-236", *Journal of Physical Review C*, **29**, 985 (1984).

Mirzadeh, S., P. P. Parekh, S. Katcoff, and Y. Y. Chu, "Cross-section Systematics for Nuclide Production at a Medium Energy Spallation Neutron Facility", *Journal of Nuclear Instruments and Methods*, **216**, 149 (1983).

Bloomer, W. D., W. H. McLaughlin, R. Milius, M. R. Zalutsky, S. J. Adelstein, S. Mirzadeh, R. M. Lambrecht, and A. P. Wolf, "Astatine-211: Optimization for Production of Inorganic Radiopharmaceuticals", *Journal of Nuclear Medicine*, **24**, P122 (1983).

Mirzadeh, S. and Y. Y. Chu, "A Rapid Radiochemical Separation Procedure for Mercury from Lead and Bismuth Targets", *Radiochemical and Radioanalytical Letters*, **51**, 279 (1982).

S. Mirzadeh

Publications in referred journals

Mirzadeh, S., M. Kahn, P. Grant, and H. A. O'Brien, Jr., "Studies of the Chemical Behavior of Carrier-free Ge-68: I. Purification by Distillation from Acidic Chloride Solutions", *Radiochimica Acta*, **28**, 47 (1981).

Mirzadeh, S., M. Kahn, P. Grant, and H. A. O'Brien, Jr., "A Procedure for the Preparation of Chloride-free Solution of Carrier-free Ge-68", *Radiochemical Radioanalytical Letters*, **42**, 361 (1980).

Grant, P. M., H. A. O'Brien, Jr., and S. Mirzadeh, "Premature Evaluation of a Ge(68)-Ga(68) Distillation Generator", *Journal of Nuclear Medicine*, **21**, 702 (1980).

Awarded Patents

DePaoli D. W., Hu, M. Z., Mirzadeh, S. and Clavier, J. W., "Inorganic Resin For Clinical Use of Bismuth-213 Generators", U. S. Patent 7,914,766 B1, March, 29, 2011.

Mirzadeh, S. and Garland, M., "Production of Thorium-229 Using Helium Nuclei" U. S. Patent 7,852,975 B2, December 14, 2010.

Knapp, F. F., Boll, R.A., Mirzadeh, S., "Chromatographic Extraction with Di(2-Ethylhexyl)-orthophosphoric Acid for Production and Purification of Promethium-147", U.S. Patent 7,435,399 B2, October 14, 2008.

Mirzadeh, S., Du, M., Beets, A. L. and Knapp, F. F., "Method for Preparation of High Specific Activity Platinum-195m for Medical Therapy", U. S. Patent 6,751,280, June 15, 2004.

Mirzadeh, S., Du, M., Beets, A. L. and Knapp, F. F., "Method for Preparing High Specific Activity Lutetium-177 ", U. S. Patent 6,716,353 B1, April 6, 2004.

Mirzadeh, S., Knapp, F. F. Jr., and Collins, E. D. "*A tandem generator for preparation of highly concentrated ⁹⁹Tc from low specific activity of ⁹⁹Mo*" U. S. Patent No., 5,729,821, March 1998.

Beets, A. L., Mirzadeh, S., Knapp, F. F. and Guhlke, S., "Concentration of Perrhenate and Pertechnetate Solutions", U.S. Patent No. 5,774,782, June 1998.

Knapp, F. F., E. C. Lisic, S. Mirzadeh, and A. P. Callahan, "*Tungsten-188/Carrier-free Re-188 Perrhenic Acid Generator System*", U.S. Patent No. 5,186,913, April 26, 1991.

Mirzadeh, S. and R. M. Lambrecht, "*Methods for the Simultaneous Preparation of Radon-211 and Xe-125, Astatine-211, Iodine-125 and Iodine-123*", U.S. Patent No. 4,644,869, May 12, 1987.

Mirzadeh, S. and R. M. Lambrecht, "*Process for Producing Astatine-211 for Radiopharmaceutical Use*", U.S. Patent No. 4,681,727, July 21, 1987.

Mirzadeh, S., R. E. Whipple, P. M. Grant, H. A. O'Brien, Jr., "*Evaporation-Based Ge/Ga(68) Separation*", U.S. Patent No. 4,268,730, February 3, 1981.

Patent Applications

Mirzadeh, S. and Garland, M., "Production of Thorium-229 from Radium-228", U.S. Patent Application Serial No. 11/507,168, Filing date: August 21, 2006 (UTB #1273.2). Not granted

Mirzadeh, S. and Garland, M., "Production of Thorium-229 from Thorium-230", U.S. Patent Application Serial No. 11/507,152, Filing date: August 21, 2006 (UTB# 1273.3.). Not granted

Mirzadeh, S. and Garland, M., "Production of Thorium-229 from Radium-226 Using Epithermal and Higher Energy Neutron Irradiation". Filing date, July, 2007 (UTB# 1273.5). Not granted

Mirzadeh, S., Aaron, S., and Zevenbergen, L. "A New Indium-114m Brachytherapy Source", U. S. Patent Application (1999). Not granted

Mirzadeh, S. and Kennel, S. J., "Vascular Targeting of Alpha Particle Emitting Radioisotopes for Radiotherapy", U.S. Patent Application (1998). Not granted