

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AdvanCell Pty Ltd.
Petitioner

v.

Sciencons AS and ARTBIO, Inc.
Patent Owner

Post Grant Review No.: PGR2025-00029

**PETITIONER'S REPLY TO PATENT OWNER RESPONSE TO POST
GRANT REVIEW OF U.S. PATENT NO. 12,125,603**

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Exhibit No.	Description
1001	U.S. Patent Number 12,125,603.
1002	Declaration of Saed Mirzadeh.
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. 12,125,603.
1007	US Patent Application Publication No. 2018/0047474 A1 (“ O’Hara ”).
1008	Hassan, Ahmed and Alnaser, Ibrahim Abdullah, “A Review of Different Manufacturing Methods of Metallic Foams” ACS Omega 2024 9 (6), 6280-6295 DOI: 10.1021/acsomega.3c08613 (“ Hassan ”).
1009	Lefebvre, Louis-Philippe, Banhart, John, and Dunand, David C., “Porous Metals and Metallic Foams: Current Status and Recent Developments,” Advanced Engineering Materials, 10, September 9, pp. 775-787, 2008 https://doi.org/10.1002/adem.200800241 , (“ Lefebvre ”).
1010	U.S. Patent Number 3,087,807.
1011	“Radioisotopes,” International Atomic Energy Agency, https://www.iaea.org/topics/nuclear-science/isotopes/radioisotopes (last accessed February 11, 2025).
1012	File History of U.S. Patent Application Serial No. 18/680,605.
1013	File History of U.S. Patent Application Serial No. 18/680,372.
1014	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 ”).
1015	U.S. Patent Number 6,592,843.
1016	“O-Ring Handbook,” Parker Hannifin Corporation, https://www.hdslippers.com/cgi-bin/pdf/Catalogues/05-O-Ring-Handbook_ODE5705-EN%20Luglio%202015.pdf (last accessed March 7, 2025).
1017	Declaration of Per Hoff.
1018	Excerpts of Merriam-Webster’s Collegiate Dictionary, 11 th ed. (2018).
1019	Declaration of Jennifer Librach Nall
1020	U.S. Patent Number 12,394,533.

Exhibit No.	Description
1021	Conroy Exhibit 3: Fraiser Kansteiner, “Nucleus RadioPharma Links Up With ARTBIO to Help Produce Prostate Cancer Candidate for Clinical Trials,” Fierce Pharma (May 7, 2024), https://www.fiercepharma.com/pharma/nuclear-medicine-cdmo-nucleus-links-artbio-help-produce-prostate-cancer-radiotherapy .
1022	Conroy Exhibit 4: ARTBIO, “ARTBIO and Nucleus RadioPharma Announce Collaboration to Manufacture GMP-Grade Therapeutic Products Containing Radioisotope Pb-212 to Support Emerging Clinical Trials” (May 7, 2024), https://artbio.com/artbio-nucleus-radiopharma-collaboration-manufacture-gmp-grade-therapeutic-products-radioisotope-pb-212-support-emerging-clinical-trials .
1023	Conroy Deposition Transcript.
1024	National Library of Medicine, “Study of Alpha Radioligand Therapy AB001 in Patients With Metastatic Castration Resistant Prostate Cancer (mCRPC) (ARTISAN)” (last updated Apr. 7, 2026), https://clinicaltrials.gov/study/NCT07214961
1025	ARTBIO, “ARTBIO Announces Dosing of Two Cohorts with AB001 in ARTISAN, a Phase 1 Alpha Radioligand Therapy Clinical Trial for Metastatic Castration Resistant Prostate Cancer” (Jan. 12, 2026), https://artbio.com/ARTBIO-Announces-dosing-of-Two-Cohorts-with-AB001
1026	ARTBIO, “ARTBIO and Nucleus RadioPharma Announce Collaboration to Manufacture GMP-Grade Therapeutic Products Containing Radioisotope Pb-212 to Support Emerging Clinical Trials” (May 7, 2024), https://artbio.com/artbio-nucleus-radiopharma-collaboration-manufacture-gmp-grade-therapeutic-products-radioisotope-pb-212-support-emerging-clinical-trials .
1027	U.S. Patent No. 12,406,776

I. INTRODUCTION

PO makes no meaningful argument for why the D.I. was incorrectly decided. The Board should find the challenged claims unpatentable.

II. CLAIM CONSTRUCTION

A. “precursor isotope source”

PO explicitly states that “no construction is believed necessary” for this term, but then proposes to limit it to require that the entire “precursor isotope source” be capable of radioactive decay; in other words, that the source consists of only radioactive material. POR, 10-12. However, as correctly recognized in the D.I., the ’603 patent states that the precursor isotope source “can be in different forms, sizes and shapes depending on the application type” (EX1001, 7:59-60) and that “[t]he source may or may not contain a holder for the radioactive part and a grid or ring or similar surrounding the source” (*id.*, 10:3-5). While the latter passage is not a model of clarity, it nonetheless indicates that the source and radioactive part are not coextensive and that the source can “contain” (*i.e.*, comprise—EX1018, def. 2b) non-radioactive structures. PO’s argument to the contrary regarding this passage (POR, 13) fails because it conflates “the radioactive part” with “the source.” This passage is consistent with claim 1 of a continuation of the ’603 patent, which requires a source comprising a ceramic material and a radioisotope. EX1027, 21:15-17. Thus, the precursor isotope source

is not limited by the '603 patent to only the radioactive material and can also comprise a “holder” as well as other structures, such as a “grid or ring,” that surround the “holder” of the radioactive material. *Id.*, 10:1-7.

Even if the Board accepts PO’s construction that the source is limited to precursor isotopes, Ground 1 establishes unpatentability of the challenged claims by demonstrating that the ^{228}Th is radioactive material disposed on the rod by being indirectly attached, as discussed in the Petition at §IV.B.3 and below in §III.B.3.

B. “disposed on the rod”

PO rejects the Petition’s proposed construction and asserts by implication a construction that requires direct attachment to the rod. POR, 14-16. However, the Board should reject PO’s proposed narrow construction because it is contrary to the specification and reads out most disclosed embodiments. The '603 patent describes an embodiment in which the “precursor isotope source can be placed on the rod, either directly or on a strip attached to the rod.” EX1001, 8:12-13, 3:54-58, 8:58-65. Contrary to PO’s construction, this language from the specification clearly and unambiguously equates “on the rod” with both indirect attachment via a strip and direct attachment. PO’s proposed narrow construction also reads out other disclosed embodiments in which the source is indirectly disposed on the rod

via a sponge, wool, or sphere. EX1001, 8:14-17, 10:31-37. A claim term is not normally construed to exclude disclosed embodiments. *Apple Inc. v. Int’l Trade Comm’n*, 169 F.4th 1363, 1382 (Fed. Cir. 2026). This principle is applicable here because there is no lexicography or disclaimer in the prosecution history that supports PO’s narrow construction that excludes these disclosed embodiments.

PO’s proposed construction should also be rejected because it cannot be reconciled with claims 8, 9, or 17. Claim 9 depends from claim 1 and requires that the source is both *disposed on a rod* (claim 1) and “*disposed in* a sponge, a wool, a strip, or a sphere.” The specification indicates that embodiments with these materials have a source that is not in direct contact with the rod. EX1001, 10:31-37 (“The second part of the assembly can, optionally, comprise a needle, rod or strip which may be supplied with a small ball of a material that can absorb radium or thorium including glass, wool, quartz wool, mineral wool, metal, paper, cotton, stearate or another fatty acid, metal, cellulose, natural mineral, polymer, ion exchange resin, or other fibrous material.”). Because it is the wool, etc. that directly contacts the rod, under PO’s construction there is no precursor isotope source “disposed on the rod” in those embodiments. A construction that excludes dependent claims should be rejected. *Baxalta Inc. v. Genentech, Inc.*, 972 F.3d 1341, 1346 (Fed. Cir. 2020) (rejecting a narrow construction that excluded

embodiments in dependent claims, stating this “weighs heavily” against the narrow construction).

The correct construction of “disposed on” is the one proffered in the Petition—directly or indirectly attached to the rod. Pet., 3. This construction is in accordance with the dictionary definition and the plain meaning. The plain and ordinary meaning of “on” is broad and includes “a source of attachment or support.” EX1018 (“on” dictionary definition (def. 2a)). Likewise, the plain and ordinary meaning of “dispose” includes “to put in place.” EX1018 (“dispose” dictionary definition (def. 2a)). None of these plain and ordinary meanings requires a direct connection. For example, consider a hanging pot that is hanging from a ceiling hook. The pot is disposed on the hook, even though the attachment is indirect, i.e., via a chain or rope. Thus, the plain and ordinary meaning of “disposed on” includes indirect connections.

PO fails to explain why Hassfjell-Hoff’s packets in a basket threaded onto the rod are not “located on” and “positioned on” the rod when the requirement for direct contact is rejected. POR, 25-26. The packets are “disposed on” the rod because the packets move with the rod (e.g., when the rod goes up, the packets do too) as admitted by PO’s expert. EX1023, 88:16-89:17. In the ’603 patent, in some embodiments, the source is deposited on a strip and then that strip is attached to the

rod. EX1001, 8:58-65. The source in that embodiment is “disposed on” the rod because the rod provides the support for the strip. That embodiment discloses that the source is *indirectly* “supported by or suspended from” the rod. This plain meaning also coincides with the specification’s description of the source being suspended in wool that is attached to the rod without the source itself being in contact with the rod. EX1001, 10:31-37.

PO’s argument that Petitioner is substituting claim terms with different terminology (POR, 14-15) is nonsense because it conflates construing a claim with redrafting it.

Nothing in PO’s argument or case citations explains why “located on” or “positioned on” the rod requires direct contact with the rod. Even cases that PO cites reject a requirement for direct contact. *Junk Food Custom Arcades, LLC v. Hit Box, LLC*, 2023 WL 11884772, *7 (N.D. Ga. Apr. 11, 2023) (construing “disposed on” to require “located or positioned” and rejecting narrower construction of “placed in contact with,” because “‘disposed on’ simply describes the relative location”); *360Heros, Inc. v. GoPro, Inc.*, 2019 WL 4894555, *5-6 (D. Del. Oct. 4, 2019) (construing “disposed on” to be “located thereon”/“located on,” and rejecting narrower construction of “placed and oriented upon the surface of”).

For these reasons, PO's narrow construction should be rejected, and the Petition's "directly or indirectly attached" construction should be adopted.

To the extent the Board construes this limitation as requiring a direct connection between the source and rod, which it should not, that connection is disclosed in Hassfjell-Hoff because, as demonstrated in the Petition, the source can be the basket and all of its contents, and the basket is directly connected to the rod via a threaded connection. Pet., 17 ("Alternatively, and additionally, the combination of the [^{228}Th]barium stearate packets and basket is the *source* of the precursor isotope in Hassfjell-Hoff, and those are directly connected to the rod.").

C. "allowing sufficient time for the precursor isotope source to decay comprises allowing 5 hours, 10 hours, 20 hours, 24 hours, 48 hours, 72 hours, or 96 hours" (claim 10)

PO essentially agrees with the Petition that this term should be construed to mean "allowing sufficient time for the precursor isotope source to decay comprises allowing at least 5 hours." POR, 16-17. In a non-sensical response during deposition that evidences that his opinion lacks credibility and should be given no weight (§IV.B), Mr. Conroy stated that claim 10 would be satisfied by allowing any amount of time to decay, whether more or less than 5 hours. EX1023, 76:10-78:4.

D. “the precursor isotope source is configured to decay and emanate the one or more progeny isotopes into the container for 5 hours, 10 hours, 20 hours, 24 hours, 48 hours, 72 hours, or 96 hours” (claim 20)

PO proposes that the time limits in this limitation should be construed the same way as the agreed construction for claim 10. However, this limitation uses significantly different language than claim 10. Specifically, instead of claim 10’s open-ended words “allowing” and “comprises allowing,” claim 20’s limitation uses the restrictive terminology “is configured” and “for.” Dr. Mirzadeh explains that a POSITA would have understood claim 20’s limitation to require exact times, while understanding claim 10’s limitation to be open-ended. EX1002, ¶¶38-39. Mr. Conroy, who is not a POSITA (§IV.B), does not explain his opinion that the claim language difference has no impact on the construction. EX2002, ¶50. His opinion is therefore entitled to no weight. *Upjohn Co. v. Mova Pharm. Corp.*, 225 F.3d 1306, 1311 (Fed. Cir. 2000) (“there must be factual support for an expert’s conclusory opinion”).

E. Limitations 1a and 1d

In its arguments regarding Ground 1, PO implies that limitations 1a and 1d require that sliding the rod must be the sole cause of the exposure and isolation of the source from the interior surface of the container. POR, 19-24. However, as

correctly preliminarily rejected (D.I., 18), there is no support for this narrow construction.

Claim 1 is a comprising claim, not a consisting of claim, and PO has no explanation for why it should be construed narrowly to require the sliding of the rod to be the **sole** cause of exposure and isolation. *CIAS, Inc. v. Alliance Gaming Corp.*, 504 F.3d 1356, 1360 (Fed. Cir. 2007) (“‘comprising’ is inclusive or open-ended and does not exclude additional, unrecited elements or method steps”).

PO argues, based on the Examiner’s Notice of Allowance, that the rod “can operate the exposure in an open or closed configuration.” POR, 23. But this language does not appear in the claim, and PO cannot show lexicography, disclaimer or disavowal.¹ In fact, PO explicitly stated that those statements were not binding and “should not be imputed to the Applicant”:

¹ Examiner statements do not constitute disclaimer. *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1124 (Fed. Cir. 2004); *Bell Atl. Network Servs., Inc. v. Covad Comm’c’ns Grp., Inc.*, 262 F.3d 1258, 1273 (Fed. Cir. 2001) (Holding that, unlike the statement of an applicant, the statements of an examiner will not necessarily limit a claim.).

Applicant has received the Examiner's Statement of Reasons for Allowance with the August 6, 2024 Notice of Allowance and Allowability regarding the above-identified application. Entry of the Statement into the record should not be construed as any agreement with or acquiescence in the reasoning stated by the Examiner. Each of the claims stands on its own merits and is patentable because of the combination it recites and not because of the presence or absence of any one particular element.

The Examiner's Statement was not prepared by Applicant and only contains the Examiner's possible positions in one or more reasons for allowability. Thus, any interpretation with respect to the Examiner's Statement of Reasons for Allowance should not be imputed to the Applicant.

EX1006, 295. This statement by the Applicant makes clear that the Examiner's statement is not an express disclaimer, disavowal, or lexicography. In any event, this language does not support PO's construction because it says nothing about the sliding of the rod being the *sole* determinant of whether the rod is exposed or sealed off as required by PO's implied construction.

Moreover, the prosecution of related patents evidences that the PO knows how to claim that sliding the rod on which a source is disposed is the *sole* determinant of whether the interior surface of the container is exposed to the source. Specifically, claim 16 of related U.S. Patent No. 12,394,533 requires a valve configured such that movement of the source causes the valve to open or close to expose the interior of the container to the source:

16. A system for generating radioisotopes comprising:
a precursor isotope source configured to move between an open position and a closed position; and

a valve configured to seal and isolate the precursor isotope source from an interior surface of a container when the precursor isotope source is in the closed position, **wherein the valve is configured such that moving the precursor isotope source from the closed position to the open position opens the valve to expose the interior surface of the container to the precursor isotope source.**

EX1020 at claim 16 (emphasis added). In contrast, neither independent claim of the '603 patent requires a specific configuration of the valve.

PO's implied construction is not supported and should be rejected.

III. ALL CHALLENGED CLAIMS ARE UNPATENTABLE

A. PO Does Not Dispute Unpatentability Under the Board's Preliminary Analysis for Grounds 1-3

The POR only addresses patentability for Grounds 1-3 under its own construction of “disposed on the rod” and “sliding the rod” (in limitations 1a and 1d), and does not dispute that Grounds 1-3 establish unpatentability for all the challenged claims under the Board's preliminary analysis rejecting those arguments. PO has therefore waived any arguments under the Board's preliminary constructions. Paper 12, 10 (arguments not raised in POR may be deemed waived). For all the reasons explained in the Petition, and as the D.I. preliminarily determined, all claims challenged in Grounds 1-3 should be found unpatentable.

B. PO Fails to Distinguish Any Elements in Ground 1

As explained below, all of PO's attempts to distinguish the disclosures of Hassfjell-Hoff fail.

1. Limitation 1a is disclosed by Hassfjell-Hoff

PO disputes whether Hassfjell-Hoff discloses limitation 1a, which requires “exposing an interior surface of a container to a precursor isotope source by sliding a rod from a closed position in which the precursor isotope source is sealed off from the interior surface of the container to an open position in which the precursor isotope source is exposed to the interior surface of the container.” POR, 18-24.

As explained in the Petition, Hassfjell-Hoff discloses limitation 1a. In Hassfjell-Hoff, when its tube (rod) is lowered from the upper chamber to the lower chamber, the basket of packets of [²²⁸Th]barium stearate is positioned inside the polyethylene bottle (the claimed “container”) and decay products deposit on the walls of the bottle:

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

EX 1003, 7; Pet., 15-16. This configuration corresponds to the “open position” as mapped in the Petition to the claim. Pet. 15; §II.E. It is undisputed that Hassfjell-Hoff teaches that (1) the exposure of the precursor isotope source to the interior

surface of the polyethylene bottle occurs in this open position, and that (2) the device's intended use includes sliding the tube/rod from the closed position to the open position for the purpose of exposing the collector surface to the precursor isotope source. Pet., 16. That some exposure also occurs as soon as the gate valve is opened before the tube/rod is lowered does not negate the Petition's showing. Hassfjell-Hoff teaches sliding the tube/rod downward such that the basket is within the polyethylene bottle, which is "an open position in which the precursor isotope source is exposed to the interior surface of the container," in order to fully expose the interior surface of the container to the source. Pet., 16. The fact that the gate valve must be opened prior to lowering the rod does not preclude limitation 1a from reading on Hassfjell-Hoff because claim 1 recites the open-ended "comprising" transition phrase and does not preclude additional steps.

Additionally, Hassfjell-Hoff's source is disposed on the rod as discussed above in §II.B (claim construction of "disposed on the rod"). Thus, Hassfjell-Hoff teaches limitation 1a when that limitation is correctly construed as discussed above.

2. Limitation 1d is disclosed by Hassfjell-Hoff

PO disputes whether Hassfjell-Hoff discloses limitation 1d, which requires “isolating the precursor isotope source from the container by sliding the rod from the open position to the closed position.” POR, 18-24.

As explained in the Petition, Hassfjell-Hoff discloses limitation 1d. Pet., 18. Hassfjell-Hoff’s precursor isotope source is isolated from the container by both pulling up the tube and closing the gate valve: “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; Pet., 18. This corresponds to the claimed “closed position” as mapped in the Petition. Pet. 15. Dr. Mirzadeh explained that, in order to isolate the source from the collector in Hassfjell-Hoff, the step of raising the tube must occur before the gate valve is closed. EX2004, 71:2-17. Hassfjell-Hoff teaches that (1) the isolation of the precursor isotope source from the interior surface of the container occurs in this closed position and that (2) the device’s intended use includes sliding the rod from the open position to the closed position for the purpose of isolating the collector surface from the precursor isotope source. Pet., 18. That the gate valve must also be closed in addition to the rod being raised does not preclude limitation 1d from reading on Hassfjell-Hoff because claim 1 uses the open-ended “comprising” transitional phrase. Thus,

Hassfjell-Hoff teaches limitation 1d under the correct construction of that limitation as discussed above.

3. “precursor isotope source disposed on the rod” is disclosed by Hassfjell-Hoff

PO argues that Hassfjell-Hoff does not disclose a “precursor isotope source disposed on the rod” because (1) Hassfjell-Hoff’s [^{228}Th]barium stearate is “not attached to anything” (POR, 24-26), and (2) [^{228}Th]barium stearate is the only disclosed “source” (POR, 26-30). Neither argument withstands any scrutiny.

PO’s theory is premised on its narrow construction of “disposed on the rod” that requires the source to be directly attached to the rod and its narrow construction of “source” as limited to radioactive material. As explained above, these constructions should be rejected. §II.A-B. PO’s admission that Hassfjell-Hoff’s packets of [^{228}Th]barium stearate are in a basket that is connected to the end of the tube (POR, 26) is dispositive—the packets are indirectly disposed on the rod—nothing more is required by the claims.

If PO’s assertion that the source is limited to the [^{228}Th]barium stearate is correct (it is not, §II.A), then Hassfjell-Hoff’s disclosure that [^{228}Th]barium stearate is placed in packets in a basket and that basket is attached to the tube using threads is an express disclosure of the source indirectly “disposed on the rod.” The [^{228}Th]barium stearate is indirectly “on” the rod because the rod is the substrate

supporting and controlling the position of the [²²⁸Th]barium stearate in Hassfjell-Hoff's device. In other words, movement of Hassfjell-Hoff's tube controls the movement of the [²²⁸Th]barium stearate, because the [²²⁸Th]barium stearate is "on" the tube (via an indirect connection, due to its placement in the packets that are in the basket that is directly disposed on the tube/rod).

If PO's assertion that "disposed on" requires direct connection is correct (it is not, §II.B), then Hassfjell-Hoff's disclosure of a basket attached to the tube (i.e., disposed on the rod), where the basket includes packets of [²²⁸Th]barium stearate, discloses the basket as a source. Pet., 17. The basket is directly "disposed on the rod." *Id.*

4. Claim 12's open and closed position requirement is disclosed by Hassfjell-Hoff

PO disputes whether Hassfjell-Hoff discloses the requirement for sliding between open and closed positions in claim 12. POR, 23-24. PO argues that claim 12 requires that movement of the rod alone "determine whether the rod is exposed or sealed off." POR, 23. However, PO proffers no claim construction that supports that requirement, and the intrinsic evidence does not support such a narrow construction. §II.E.

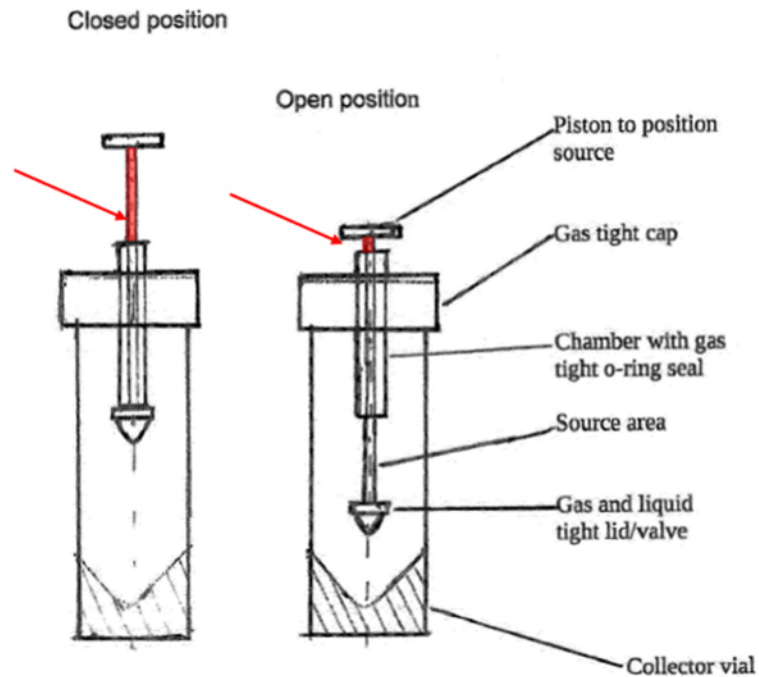
As explained in the Petition, Hassfjell-Hoff discloses a rod that is configured to slide between an open position and a closed position. Pet., 31-32. Specifically,

the rod in Hassfjell-Hoff slides between an open position and a closed position by pulling the Hassfjell-Hoff tube up out of the collector chamber and closing the gate valve. *Id.*; §III.B.1. This evidence discloses what is required by claim 12—the rod slides between an open and a closed position.

5. Hassfjell-Hoff discloses o-rings that form a gas tight seal between the rod and the tube as required by claims 5, 14, and 15

PO's theories in its POR §V.A.3 are hard to parse and do not make much sense. POR, 31-34.

PO might be arguing that Claim 5 is not disclosed because Hassfjell-Hoff's o-ring seals between the Hassfjell-Hoff's tube (*i.e.*, the claimed rod) and Hassfjell-Hoff's tube passage (*i.e.*, the claimed tube) does not seal the **entire** rod "within" the claimed tube. POR, 31-33. However, such a narrow construction would exclude the only disclosed embodiment of the '603 patent, Figure 4. In Figure 4, the entire rod is **never** fully sealed "within" the tube (referred to as a "chamber" in Figure 4). In both the open and closed positions in Figure 4, a portion of the rod (shown below in red) extends above the o-ring seals which are necessarily located within the tube/chamber.



EX1001, Fig. 4 (annotated). Thus, a narrow construction of “within” is unsupported by the specification and should be rejected. Moreover, PO’s proposed construction renders the claim invalid under §112 because such a device is not enabled and lacks written description support in the specification. And, it is undisputed that Hassfjell-Hoff discloses a rod with a portion that is partially sealed within a tube that uses gas-tight o-ring seals. PO’s arguments about claim 5 should be rejected.

For claim 14, PO apparently argues that “to isolate” modifies “seal” (which is ironic given PO’s arguments about the doctrine of last antecedent in the ’437 PGR). POR, 33. Yet, Hassfjell-Hoff literally discloses this claim limitation. PO

does not deny that the Hassfjell-Hoff device has a “rod [that] forms a gas tight seal with a tube” and that Hassfjell-Hoff’s “rod slides to isolate the precursor isotope source from the interior surface.” And, Hassfjell-Hoff’s seal to the outside environment also isolates the precursor isotope source from the interior surface when the container is being replaced/removed from the lower chamber.

To the extent that PO is arguing that the claim requires that sliding the rod must be the only action that is required for the rod to form a gas tight seal with a tube, such a narrow construction is not supported by the intrinsic evidence. Figure 4 of the '603 patent has o-rings and a valve that are **both** gas-tight seals required for the chamber to be gas tight. For the same reasons that Hassfjell-Hoff discloses “by sliding the rod,” it also discloses claim 14’s “rod slides to isolate.” §III.B.1. In Hassfjell-Hoff, when its tube (rod) is lowered from the upper chamber to the lower chamber, the [²²⁸Th]barium stearate is positioned inside the polyethylene bottle (container) and decay products deposit on the walls of the bottle. EX1003, 7; Pet., 15-16. Hassfjell-Hoff’s source is then able to be isolated from the container by both pulling up the tube and closing the gate valve. EX1003, 7; Pet. 15-16. Dr. Mirzadeh explained that, in order to isolate the source from the collector in Hassfjell-Hoff, the step of raising the tube must occur before the gate valve is

closed. EX2004, 71:2-17. Thus, as explained in the Petition, claim 14 is disclosed by Hassfjell-Hoff and PO's arguments should be rejected.

For claim 15, PO's argument assumes a construction that is unreasonably narrow and unsupported by intrinsic evidence. It seems that PO argues that claim 15 requires the rod and o-rings to be disclosed as a single component, and the rod is not allowed to slide through the o-rings. POR, 33-34. Yet, the '603 patent only discloses a rod and o-rings as two components that are used together ("using an O-ring") such that the rod slides through the o-rings. Thus, PO's narrow construction of claim 15 is unsupported by the intrinsic evidence and should be rejected. It is undisputed that Hassfjell-Hoff discloses o-rings that form a gas tight seal between the rod and tube when the system is in the closed position. POR, 33 ("the O-ring is affixed to the tube passage"). Moreover, PO's proposed construction renders the claim invalid under §112 because such a device is not enabled and lacks written description support in the specification. In summary, PO's arguments about claim 15 should be rejected.

6. Hassfjell-Hoff discloses the limitations of claims 8 and 17

PO's argument is premised on its "disposed on the rod" construction (POR, 34-35). This construction is wrong because it excludes some embodiments of these claims in the '603 patent. §II.B. Instead, the source in the '603 patent can be

indirectly disposed on the rod because it is inside a gas permeable barrier (*e.g.*, wool or strip) and the source emanates through the barrier. PO identifies no arguments that these claims are not disclosed if its claim construction is rejected.

C. PO Fails to Distinguish Any Elements in Ground 2

The POR only addresses patentability under its own constructions. POR, 35-37. Under Petitioner's constructions, all the challenged claims are indisputably unpatentable.

D. PO Fails to Distinguish Any Elements in Ground 3

PO seems to misunderstand the proposed combination. Petitioner does not propose, as PO posits, putting the filering basket and its contents in a sponge. The Petition proposes *replacing* the filering basket and its contents with the sponge of O'Hara. Pet., 53 (a POSITA would "implement the filter membrane packets and surrounding filering basket disclosed by Hassfjell-Hoff with the O'Hara gas permeable metal or mineral membrane, screen, filter, or porous disc (each are a sponge) containing the precursor isotope source."). PO admits that O'Hara supports this proposed combination. POR, 38 ("O'Hara at best supports disposing radioactive isotopes in various materials."). Therefore, PO has failed to show any flaws in the obviousness analysis in Ground 3.

E. Ground 4 Proves Certain Claims Unpatentable

1. Claims 2 and 3 are invalid under §112

Encompassed within the scope of claim 2 are three situations: (1) ^{228}Th ; (2) ^{224}Ra ; and (3) ^{228}Th and ^{224}Ra . EX1001, cl. 2 (“exposing the interior surface to a thorium 228 isotope (^{228}Th) and/or a radium 224 isotope (^{224}Ra)”); EX1023, 90:18-91:16 (Mr. Conroy agreeing that claim 2 covers all three scenarios “together or in singular”). The 35 U.S.C. §112 enablement requirement means that the specification must support the full breadth of these claims (*i.e.*, all three situations)—and not merely one of them. *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1346 (Fed. Cir. 2005) (“[D]escription of one method . . . does not entitle the inventor . . . to claim any and all means for achieving that objective.”). PO does not deny that situation 1 is not enabled by the ’603 patent (POR, 42-44), therefore claims 2 and 3 are invalid under §112.

2. Claim 20 is invalid under §112

As explained in the Petition and above in §II.D, claim 20 should be construed to require exactly one of the listed times. Dr. Mirzadeh’s proposed construction is the only one supported by a POSITA, because Mr. Conroy is not qualified to opine in this field. Moreover, PO does not deny that the claim is invalid under §112 to the extent the Board adopts this construction. POR, 51-53

IV. EXPERTS

A. Petitioner's Experts

PO's complaints concerning Petitioner's experts are without merit.

1. Per Hoff

Per Hoff provided a detailed declaration that explained exactly how the device in his article actually worked at the time. EX1017, ¶¶32-37. PO does not take issue with his statements regarding how the device worked or dispute that he is a POSITA.

2. Dr. Mirzadeh

PO's assertion that Dr. Mirzadeh copied the Petition is directly contradicted by Dr. Mirzadeh's sworn testimony that he drafted his declaration (except for the legal standards). EX2004, 12:14-13:7, 73:18-75:20. Finally, PO does not dispute that Dr. Mirzadeh is a POSITA.

B. PO's Expert Declaration Deserves No Weight

PO and Mr. Conroy do not dispute Petitioner's POSITA definition. *See generally*, POR; EX2002, ¶33; EX1023, 60:2-8. Yet, under that definition, Mr. Conroy is not a POSITA.

“To offer expert testimony from the perspective of a skilled artisan in a patent case—like for claim construction, validity, or infringement—a witness must at least have ordinary skill in the art.” *Kyocera Senco Indus. Tools Inc. v. Int'l*

Trade Comm’n, 22 F.4th 1369, 1376-77 (Fed. Cir. 2022). “Without that skill, the witness’ opinions are neither relevant nor reliable.” *Id.* at 1377. “General experience in a related field may not suffice when experience and skill in specific product design are necessary to resolve patent issues.” *Extreme Networks, Inc. v. Enterasys Networks, Inc.*, 395 F. App’x 709, 715 (Fed. Cir. 2010).

The ’603 patent describes a highly technical method and system for producing ^{212}Pb by isolating and purifying it through a comprehensive decay chain. A POSITA opining on claim construction and validity must have **relevant** experience with radioisotope generators, not merely their marketing and use for pharmaceutical dispensing. Pet, 2-3; *Calco v. Ossur Ams., Inc.*, 2026 WL 939211, *4 (C.D. Cal. Apr. 2, 2026) (excluding expert who did not have development experience and holding that “[d]rafting patent applications . . . is not the same as developing the goods oneself”).

Mr. Conroy is not a POSITA. Mr. Conroy has neither a bachelor’s degree in “chemistry, chemical engineering, physics, nuclear chemistry, radiochemistry, or materials science” or a comparable field of study, nor **relevant** professional experience with radioisotope generators. Pet., 2-3; EX1023, 17:23-18:9. Mr. Conroy has an MBA and a degree in Pharmacy, and is a radiopharmacist with experience in *using* radioisotope generators (although never emanation-based

generators which are at issue here - EX1023, 85:22-24) and *marketing* and *business administration* for radioisotope generator companies. EX2002, ¶2, 4. He conceded that he did not take any coursework on radioisotope generators while studying for his MBA, never performed scientific research in the radiopharmaceutical field, and never designed a radiopharmaceutical generator. EX1023, 17:19-22, 19:3-9. In the same way that using a Keurig or espresso machine does not make one an expert on coffee brewing machines, Mr. Conroy's experience using isotope generators cannot confer POSITA eligibility here. And marketing experience cannot substitute for technical expertise. For example, in *Grantley Patent Holdings, Ltd. v. Clear Channel Communications, Inc.*, the district court excluded the opinions of an "expert" with "an M.B.A. in marketing and forty years in the radio industry in marketing and as a program director" because he never "develop[ed]" the patented technology or anything like it. 2008 WL 7701186, *3 (E.D. Tex. Apr. 4, 2008). Thus, Mr. Conroy is not a POSITA, and his declaration is entitled to no weight. *BOE Tech. Group Co., Ltd. v. Optronics Sciences LLC*, IPR2024-01130, Paper 47 at 23 (PTAB. Jan. 26, 2026).

Furthermore, Mr. Conroy has close ties to and a financial stake related to patent owner, ARTBIO, so his declaration should be accorded little weight. In "determining the probative weight of [an expert's] testimony," the Board

“consider[s] his status as an interested witness.” *Parrot S.A. v. QFO Labs, Inc.*, IPR2018-01690, Paper 40 at 63-64 (PTAB Feb. 20, 2020). An expert witness is “interested” if he has a “financial stake” in the outcome of the case. *Id.* (attributing “little or no weight to [the expert’s] testimony” where he had financial interest in the validity of the patent at issue); *Ethicon, Inc. v. U.S. Surgical Corp.*, 135 F.3d 1456, 1465 (Fed. Cir. 1998) (“[A] witness’s pecuniary interest in the outcome of a case goes to the probative weight of testimony.”). For example, in *Transcend Medical, Inc. v. Glaukos Corp.*, the district court gave “little weight” to an expert who owned stock in the patentee company and otherwise had “close ties to and significant financial interests” in the patentee. 2015 WL 263612, *7 (D. Del. Jan. 16, 2015).

Mr. Conroy has close ties and significant financial interests related to this patent’s exclusive licensee, ARTBIO, and the validity of the ’603 patent. Mr. Conroy founded Nucleus RadioPharma (“Nucleus”) in 2022 and was its CEO from its founding until June 30, 2025. EX2002, ¶7; EX2003, 2. Though he has left Nucleus, Mr. Conroy [REDACTED] [REDACTED] EX1023, 51:3-17, 221:20-222:22. In May 2024, Nucleus obtained its first commercial partnership: the ’603 patent’s exclusive licensee, ARTBIO. EX1021; EX1022; EX1023, 59:5-11. Mr. Conroy was “thrilled to unite”

with ARTBIO in a “strategic partnership.” EX1022, 2. Per their partnership, Nucleus would “manufacture ARTBIO’s ^{212}Pb -radiolabeled therapies for its planned Phase I and II clinical trials of its lead program in prostate cancer, AB001, using ARTBIO’s proprietary AlphaDirect™ ^{212}Pb isolation technology.” EX1026. Those clinical trials are ongoing. EX1024 (describing active clinical trials of AB001 by ARTBIO); EX1025 (describing these trials as way to “develop[] a new class of ^{212}Pb alpha radioligand therapies”).

ARTBIO’s AlphaDirect™ technology is likely the commercial embodiment of the invention disclosed in the ’603 patent and related applications. The ’603 patent discloses a single chamber diffusion generator that produces ^{212}Pb in high purity from a precursor isotope source without the need for complex processing, yielding purity better than 99.8%, in a compact format suitable for shipment to end users. EX1001 at Abstract, 5:37-44, 11:3-6, 19:39-43. ARTBIO describes AlphaDirect™ in materially the same terms: as a “first-of-its-kind” ^{212}Pb isolation technology that delivers “highly pure ^{212}Pb from widely available raw materials” in a “benchtop format” with a “simple process with no separation that results in 99.9%+ purity,” using “starting materials derived from accessible nuclear industry stockpiles.” EX1026. ARTBIO itself refers to AlphaDirect™ as its “patented” technology and uses it in the manufacture of its lead therapeutic candidate, AB001,

for clinical trials in prostate cancer. EX1026. The identity of the underlying technology and ARTBIO's own public statements confirm that AlphaDirect™ is the product of the '603 patent family.

Thus, Mr. Conroy has a vested financial interest in the validity of the '603 patent. Nucleus—in which Mr. Conroy [REDACTED]— is actively manufacturing the “patented” technology being used in ARTBIO's clinical trials. Mr. Conroy has a personal interest in this ongoing “strategic” partnership, which will likely be affected by any decision to invalidate the '603 patent. Because Mr. Conroy is a biased and interested witness, the Board should give his declaration little weight.

V. CONCLUSION

The Board should find all Challenged Claims unpatentable.

Date: April 29, 2026

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CERTIFICATION UNDER 37 CFR § 42.24

Under the provisions of 37 CFR § 42.24(d), the undersigned hereby certifies that the applicable word count for the foregoing Reply to Patent Owner's Response totals approximately 5,599 as calculated by Microsoft Word, exclusive of the table of contents, mandatory notices under § 42.8, certificates of service, word count, claim listing, and exhibits which is less than the 5,600 allowed under 37 CFR § 42.24.

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that the parties have agreed that filing with the Board through the P-TACTS system constitutes electronic service and that such service as made on Patent Owner's counsel on April 29, 2026 at the following addresses:

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