

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

JUBILANT DRAXIMAGE INC.,
Petitioner,

v.

BRACCO DIAGNOSTICS INC.,
Patent Owner.

Case IPR2018-01449
Patent 9,299,467 B2

Before HYUN J. JUNG, GEORGE R. HOSKINS, and
RICHARD H. MARSCHALL, *Administrative Patent Judges*.

MARSCHALL, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
35 U.S.C. § 318(a)

I. INTRODUCTION

Jubilant DraxImage Inc. (“Petitioner”) filed a Petition (Paper 1, “Pet.”) requesting institution of an *inter partes* review of claims 1–4, 6–16, and 18–22 of U.S. Patent No. 9,299,467 B2 (Ex. 1001, “the ’467 patent”). Bracco Diagnostics Inc. (“Patent Owner”) filed a Preliminary Response (Paper 6). Pursuant to 35 U.S.C. § 314, we instituted an *inter partes* review of claims 1–4, 6–16, and 18–22 the ’467 patent, on all presented challenges. Paper 7 (“Dec. to Inst.”), 2, 21. After institution, Patent Owner filed a Response (Paper 13, “PO Resp.”), to which Petitioner filed a Reply (Paper 14, “Pet. Reply”), and Patent Owner filed a Sur-Reply (Paper 15, “PO Sur-Reply”). An oral hearing in this proceeding was held on October 29, 2019; a transcript of the hearing is included in the record (Paper 24, “Tr.”).

We have jurisdiction under 35 U.S.C. § 6. This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–4, 6–16, and 18–22 of the ’467 patent are unpatentable.

II. BACKGROUND

A. *Real Parties in Interest*

Petitioner states that the “real parties-in-interest for this Petition are Jubilant DraxImage Inc., Jubilant Pharma Limited, and Jubilant Life Science Limited.” Pet. 2. Patent Owner states that “Bracco Diagnostics Inc. (‘Bracco’) . . . is the real party-in-interest.” Paper 4, 2.

B. *Related Proceedings*

The parties indicate that the ’467 patent has been asserted in *Bracco Diagnostics Inc. v. Jubilant DraxImage Inc.*, Case No. 3-18-cv-04422

(D.N.J.). Pet. 2; Paper 4, 2; Exs. 1002, 1004. A related patent, U.S. Patent No. 9,299,468 B2, claims priority to applications in common with the '467 patent, and is the subject of challenges in IPR2018-01448 and IPR2018-01450. Pet. 2; Paper 4, 2.

The parties also indicate that the district court litigation is stayed pending resolution of Investigation No. 337-TA-1110 by the U.S. International Trade Commission (“ITC” or “Commission”). Pet. 2 (citing Exs. 1002–1004); PO Resp. 2 (citing Exs. 1002–1004); Ex. 1004 (order from civil action no. 3:18-cv-4422 granting joint motion to stay pending resolution of ITC Investigation No. 337-TA-1110).

In the ITC investigation filed March 27, 2018, Bracco Diagnostics, Inc. contends that Jubilant DraxImage Inc., Jubilant Pharma Limited, and Jubilant Life Sciences violate Section 337 of the Tariff Act of 1930 by importing strontium-rubidium infusion systems and components that infringe one or more of U.S. Patent Nos. 9,814,826; 9,750,869; and 9,750,870. Ex. 1003, 1, 14. The '467 patent is not part of the ITC investigation, but Patent Owner indicates that the investigation “involv[es] related patents.” PO Resp. 2 (citing Exs. 1002–1004). Patent Owner also states that “an ITC evidentiary hearing was held April 11–17 relative to the related patents, and many of the same factual issues disputed there are also in dispute here.” *Id.*

Patent Owner subsequently filed a “Notice of Commission Determination to Review in Part a Final Initial Determination Finding No Section 337 Violation.” Paper 19; Ex. 2018 (notice from Investigation No. 337-TA-1110 issued Sept. 30, 2019). The notice states that a Final Initial Determination (“FID”) was issued on August 1, 2019, “the FID finds . . . all

asserted claims are infringed but invalid as obvious over the prior art,” and the “Commission has determined to review the FID in part.” Ex. 2018, 2.

Petitioner filed a “Notice of Commission Final Determination of No Violation of Section 337; Termination of the Investigation.” Paper 25, 1; Ex. 1039. According to Petitioner, “Ex. 1039 indicates that the Commission determined to affirm with modification and to supplement the prior Final Initial Determination’s findings with respect to the invalidity of the patent claims asserted in the 1110 Investigation.” Paper 25, 1 (citing Ex. 1039, 2); Ex. 1039, 2 (stating that “the Commission has determined to affirm with modification and to supplement the FID’s findings with respect to the invalidity of the asserted patent claims”).

Petitioner also filed a public version of a Commission Opinion for Investigation No. 337-TA-1110. Paper 26; Ex. 1040. Petitioner states that the “Commission Opinion addresses several issues that are relevant to the present *inter partes* review.” Paper 26, 1. According to Petitioner, “the Commission considered teachings of the Klein reference against claim elements that require a computer not to allow a patient infusion when a strontium breakthrough test result is greater than or equal to an allowed limit, holding that Klein teaches or discloses such subject matter.” *Id.* (citing Ex. 1040, 24–26). Petitioner also states that “the Commission evaluated and rejected testimony from Bracco’s expert, Dr. Norbert Pelc, on several issues.” *Id.* (citing Ex. 1040, 18, 20–21, 25–26). Patent Owner has filed an appeal of the Commission Opinion. Ex. 2019.

C. The ’467 Patent (Ex. 1001)

The ’467 patent issued March 29, 2016, from an application filed August 8, 2014, which is a continuation of an application filed June 11,

provides feedback for directing the eluant via divergence valve 35WP¹ to either waste bottle 23 or patient line 305p. *Id.* at 5:4–8. Divergence valve 35BG directs eluant to either tubing line 304 to generator 21 or to by-pass tubing line 303 and patient line 305p. *Id.* at 5:35–39.

“[A]ccording to alternate embodiments, system 10 includes an ‘on board’ dose calibrator for quality control tests, and circuit 300 is expanded to include elements for an automated collection of eluate samples for activity measurements, via the on board dose calibrator,” such as “downstream of divergence valve 35WP and in communication with tubing line 305P.” *Id.* at 7:64–8:5; *see also id.* at 18:48–52 (stating “some alternate embodiments . . . include an on board dose calibrator so that the entire sequence of sample collection and calculation steps . . . for the quality control procedures, may be automated”).

Also, in some embodiments, “computer 17 is coupled to a controller of system 10” and “monitor 172 of computer 17 not only displays indications of system operation for a user of system 10, but also serves as a device for user input (e.g. touch screen input).” *Id.* at 3:22–27. The user can interact with menus on computer 17 to perform breakthrough testing. *Id.* at 16:48–51. Computer 17 may calculate and display the breakthrough test results and may also display the allowable limits for those test results. *Id.* at 17:50–54. “[S]ystem 10 will not allow an infusion if the results exceed the acceptable limits.” *Id.* at 17:57–58.

¹ The “Detailed Description” of the ’467 patent describes valve 35WP; however, Figure 1D labels the valve as “35WAP.”

D. Illustrative Claim

The '467 patent has 22 claims, of which Petitioner challenges claims 1–4, 6–16, and 18–22 in this proceeding. Of those, claims 1 and 13 are independent. Claim 1 is reproduced below.

1. A system comprising:
 - a shielding assembly configured to contain a radioisotope generator that generates radioactive eluate via elution;
 - a computer carried by the shielding assembly, wherein the computer is configured to receive a user input and, responsive to receiving the user input, control the radioisotope generator to generate a sample of eluate via elution during breakthrough testing; and
 - a dose calibrator electronically coupled to the computer and configured to measure an activity of the sample of eluate generated during breakthrough testing,wherein the computer carried by the shielding assembly is configured to receive the activity data from the dose calibrator and calculate breakthrough test results, and
the computer is further configured to prevent a patient infusion procedure if a breakthrough test result exceeds an allowable limit.

Ex. 1001, 23:48–64.

E. Evidence Relied Upon by Petitioner and Patent Owner

Petitioner identifies the following references as prior art in the asserted grounds of unpatentability:

Ran Klein, Precise ⁸²Rb Infusion System for Cardiac Perfusion Measurement Using 3D Positron Emission Tomography (2006²) (Ex. 1014, “Klein”);

U.S. Patent Application Publication No. US 2008/0177126 A1, published July 24, 2008 (Ex. 1022, “Tate”); and

Bracco Diagnostics Inc., RB-82 Infusion System User’s Guide (rev. 07, 2004) (Ex. 1021, “Bracco Manual”).

Petitioner also relies upon the Declaration of Robert T. Stone, Ph.D. (Ex. 1015) and the Declaration of Venkatesh L. Murthy, M.D., Ph.D. (Ex. 1017). Patent Owner filed a Declaration of Norbert J. Pelc, Sc.D. (Ex. 2003) and deposition transcripts for Dr. Stone and Dr. Murthy (Exs. 2010, 2016).

F. Asserted Grounds

Petitioner challenges claims 1–4, 6–16, and 18–22 on the following grounds. Pet. 23–67.

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1–4, 6, 7, 9, 10, 12–16, 18–20	102(b) ³	Klein
11, 22	103(a)	Klein, Tate

² The cover page of Klein has a February 2005 date and 2005 copyright. Petitioner contends that Klein was publicly available in 2006. Pet. 17 (citing Ex. 1020 ¶ 4, attachments B, C).

³ The relevant sections of the Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112–29, 125 Stat. 284 (Sept. 16, 2011), took effect on March 16, 2013. The application from which the ’467 patent issued was filed in August 2014, but asserts continuation priority to several applications filed before March 2013. Because there is no argument in the record to suggest the AIA version of Title 35 applies to the ’467 patent, our citations to Title 35 are to the pre-AIA version.

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
8, 21	103(a)	Klein, Bracco Manual

III. ANALYSIS

A. Legal Standards

To prevail in its challenges, Petitioner must prove unpatentability by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d).

To anticipate a claim under 35 U.S.C. § 102, “a single prior art reference must expressly or inherently disclose each claim limitation.” *Finisar Corp. v. DirecTV Group, Inc.*, 523 F.3d 1323, 1334 (Fed. Cir. 2008). That “single reference must describe the claimed invention with sufficient precision and detail to establish that the subject matter existed in the prior art.” *Verve, LLC v. Crane Cams, Inc.*, 311 F.3d 1116, 1120 (Fed. Cir. 2002).

A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the subject matter sought to be patented 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 having ordinary skill in the art to which said subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

B. Level of Ordinary Skill in the Art

Petitioner contends that a person having ordinary skill in the art would have a

graduate's degree with some emphasis in equipment design, automation, or controls, such as electrical engineering, systems engineering, mechanical engineering, or a related field, or an undergraduate degree in such fields with two to three years' work experience in radioactive protection systems or in medical device product, automation, or instrumentation design and development, including work with prototypes and finished commercial products.

Pet. 10–11 (citing Ex. 1015 ¶¶ 32–42).

Petitioner also contends that “[s]uch a person would have had a basic understanding, through education or experience, of general design control principles and processes and practices for partial or full automation of existing processes or test procedures.” *Id.* at 11 (citing Ex. 1015 ¶¶ 32–42). Petitioner further argues that Patent Owner's proposed level of ordinary skill in the related ITC case is flawed because the claims challenged in this proceeding additionally recite a computer that automates procedures previously manually performed by medical personnel and “[m]edical personnel like those suggested by the Patent Owner lack the education and experience to develop the hardware and software controls for such computer-controlled systems or to design radiation shielding.” *Id.* at 11–12 (citing Ex. 1014; Ex. 1015 § IV; Ex. 1021; Ex. 1031).

Patent Owner asserts that a person of ordinary skill in the art “would generally have a graduate degree in medicine and/or in a medical related science, including physics, chemistry, biology, physiology, and/or biophysics, and would generally have at least some clinical, research and/or design experience with respect to PET imaging and/or PET imaging

systems.” PO Resp. 3–4. Patent Owner also asserts that “[a]n individual with an undergraduate degree along with significant experience could also be sufficiently skilled,” “the amount of experience following an undergraduate degree would depend on the level of formal education and amount of experience working with radiopharmaceuticals,” and “such a person may be working as part of a team.” *Id.* (citing Ex. 2003 ¶ 27); see also *id.* at 4–5 (citing Ex. 2003 ¶¶ 27–29).

Patent Owner argues that Petitioner’s proposed level of ordinary skill “does not actually require familiarity with elution of radioactive isotopes, PET imaging, or even systems employing any form of radioactive substance.” *Id.* at 4. Patent Owner further contends that “Petitioner has failed to show that the Challenged Claims are invalid under either party’s proposed level of skill.” *Id.* at 5.

In determining the level of ordinary skill in the art, various factors may be considered, including the “type of problems encountered in the art; prior art solutions to those problems; rapidity with which innovations are made; sophistication of the technology; and educational level of active workers in the field.” *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995) (citation and internal quotation marks omitted).

Klein addresses the development of a system for eluting a constant rate of activity. See Ex. 1014, 1 (“The goal of this project is to develop a system that is capable of eluting ^{82}Rb at a constant rate of activity from a $^{82}\text{Sr}/^{82}\text{Rb}$ generator for use in a clinical and experimental setting.”). Tate states that “[i]t has long been recognized as very desirable to develop devices, systems, components and methods for calculating and delivering accurate and effective doses of radiopharmaceuticals to patients, while

reducing the exposure of administering or other medical personnel to such hazardous pharmaceuticals.” Ex. 1025 ¶ 11.

Based on the full record before us, because the asserted references describe the problems and solutions of accurately delivering radiopharmaceuticals and reducing radiation exposure to operators, we find that Petitioner’s proposed level of ordinary skill in the art, which includes understanding of equipment control, “radioactive protection systems,” and equipment design, is consistent with the prior art of record. Pet. 10–11 (citing Ex. 1015 ¶¶ 32–42). We, therefore, apply Petitioner’s proposed level of skill to our analysis.

We also determine that the parties’ competing proposals regarding the level of ordinary skill agree in certain aspects. For example, both parties propose at least a graduate degree, albeit in different concentrations of study. *See* Pet. 10 (“graduate’s degree with some emphasis in equipment design, automation, or controls, . . . or a related field”); PO Resp. 3 (“a graduate degree in medicine and/or in a medical related science”). Both parties also alternatively propose that the ordinarily skilled artisan would have had “an undergraduate degree in such fields with two to three years’ work experience in radioactive protection systems or in medical device product, automation, or instrumentation design and development, including work with prototypes and finished commercial products” (Pet. 10–11) or “an undergraduate degree along with significant experience,” “the amount of experience following an undergraduate degree would depend on the level of formal education and amount of experience working with radiopharmaceuticals” (PO Resp. 4).

We further determine that Petitioner’s proposed ordinarily skilled artisan with “an undergraduate degree in [equipment design, automation, or

controls, or a related field] with two to three years’ work experience . . . in medical device product, automation, or instrumentation design and development” (see Pet. 10–11) would overlap, at least in part, Patent Owner’s proposal of a person having “a graduate degree in medicine and/or in a medical related science” and “at least some . . . design experience with respect to . . . PET imaging systems” (see PO Resp. 3–4). We, thus, determine that any differences between the parties’ proposed level of skill would not affect our analysis below. *See also* Pet. Reply 1–2 (“Although the parties define [the person of ordinary skill in the art] differently, neither party argues that the differences between them are material to the outcome of this IPR.”).

C. Claim Construction

In the present *inter partes* review, claim terms in the ’467 patent, which is unexpired, are interpreted according to their broadest reasonable construction in light of the Specification of the ’467 patent. 37 C.F.R. § 42.100(b) (2017); *Cuozzo Speed Techs. LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016) (upholding the use of the broadest reasonable interpretation standard).⁴

Petitioner states that “[a]ll claim terms have been assigned their ordinary and customary meaning in this analysis.” Pet. 12. “Patent Owner

⁴ On October 11, 2018, the Office revised its rules to harmonize the Board’s claim construction standard with that used in civil actions under 35 U.S.C. § 282(b) in federal district court. Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018) (amending 37 C.F.R. § 42.100(b) effective November 13, 2018). This rule change does not apply here. *See* Paper 3, 1 (according filing date of August 22, 2018 to

believes that no specific constructions are required at this time” (PO Resp. 3), and Petitioner replies that “[t]here are no claim construction issues in dispute” (Pet. Reply 1). *See also* Tr. 8:14–19 (Petitioner’s counsel agreeing that no claim term in this proceeding needs express interpretation).

We agree with the parties that no express interpretation is required for any claim term. *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (construing explicitly only those claim terms in controversy and only to the extent necessary to resolve the controversy); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (applying *Vivid Techs.* in the context of an *inter partes* review).

D. Challenge Under 35 U.S.C. § 102 Based on Klein

Petitioner challenges claims 1–4, 6, 7, 9, 10, 12–16, and 18–20 as anticipated by Klein. Pet. 23–55. For these challenges, Petitioner cites to the asserted reference and Petitioner’s declarant testimony. *Id.* As discussed further below, Patent Owner argues that Klein fails to anticipate any of the claims because it fails to disclose a computer that prevents patient infusion procedures if a strontium breakthrough test result exceeds an allowable limit, as required by independent claims 1 and 13, but otherwise does not contest Petitioner’s contentions as to claims 1 and 13. PO Resp. 8–19.

After reviewing the complete record, we conclude that Petitioner has shown by a preponderance of the evidence that Klein discloses all the limitations of claims 1–4, 6, 7, 9, 10, 12–16, and 18–20.

the Petition); PO Resp. 3 (stating that the “present IPR was filed before the new IPR rules regarding claim construction were implemented”).

1. Klein (Ex. 1014)

Klein is a student thesis that “describes the development of a Rubidium-82 (^{82}Rb) infusion system for use in positron emission tomography (PET)” and “is based on a $^{82}\text{Sr}/^{82}\text{Rb}$ generator which produces ^{82}Rb activity continuously.” Ex. 1014, 1⁵; *see also id.* at 8 (“ ^{82}Rb can be supplied using a $^{82}\text{Sr}/^{82}\text{Rb}$ generator.”)

“The goal of this project is to develop a system that is capable of eluting ^{82}Rb at a constant rate of activity from a $^{82}\text{Sr}/^{82}\text{Rb}$ generator for use in a clinical and experimental setting.” *Id.* at 1. Klein “introduces the second generation ^{82}Rb elution system (RbES).” *Id.* Figure 2-2 of Klein is reproduced below. *Id.* at 19.

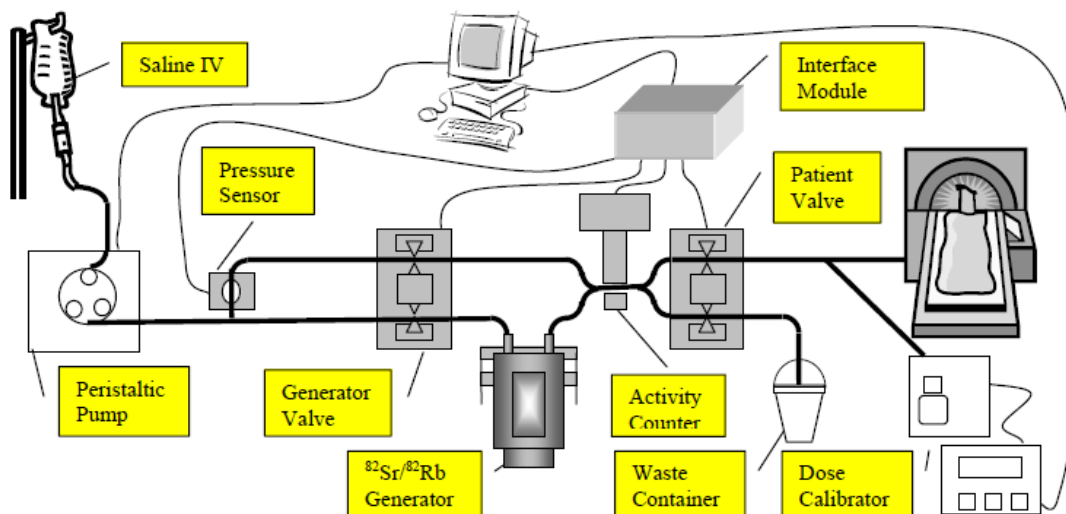


Figure 2-2 – Hardware component diagram of the RbES prototype [18] was not altered.

Figure 2-2 is a hardware component diagram of an RbES prototype. Ex. 1014, 19. Klein includes a personal computer that interfaces with sensors and actuators to allow flow of saline through a $^{82}\text{Sr}/^{82}\text{Rb}$ generator or a bypass line to the patient, dose calibrator, or waste container. *Id.* Klein

⁵ Our citations to Klein are to the page numbers found in the bottom center of each page.

states that “using a PC to control the system” allows for a “wide range of applications and devices that are readily supported” including “off-the-shelf user interface devices, as well as machine interfaces and data acquisition devices” *Id.* at 20.

“All the components are assembled in a stainless steel cart.” *Id.* at 23. The “generator was placed in the cart and surrounded by lead rings to provide maximum radiation shielding” from which “⁸²Rb is eluted in the form of ⁸²RbCl (eluate).” *Id.* at 8, 23; *see also id.* at 34 (stating that the “waste container is located on the top shelf inside the cart and is contained within lead shielding to minimize exposure to the operator”).

“All the saline lines were mounted on a modified top cover” (*id.* at 23), and “[a]lthough the generator and waste container are shielded by lead, the saline lines are a source of radiation during elutions” (*id.* at 36).

Klein also includes flow control valves, an activity counter, pumps, and a pressure sensor. *Id.* at 21–23. Klein states that “real-time software controls the pumps and valves” to “affect the flow of saline through the generator or its bypass line to the patient, dose calibrator, or waste container.” *Id.* at 19. The system acquires data from the activity counter and dose calibrator. *Id.* The “activity counter was included in the design to allow data collection and monitoring of the elution of activity” so as to “develop[] a controller capable of directing saline through the generator or its bypass line by actuating the generator valve in order to achieve a constant rate of activity using feedback from the activity counter.” *Id.* at 71.

According to Klein, the “system is required to operate in a clinical setting and therefore must be reliable, easy to operate, and above all, safe.” *Id.* at 26. Klein also states that “⁸²Sr and ⁸⁵Sr ‘breakthrough’ can result if the

generator is used indefinitely” and “[i]n high quantities these compounds may have ill effects on health.” *Id.* at 9. Klein describes that if there is an indication of excessive strontium breakthrough, then “elution to patients should be avoided.” *Id.* at 10; *see also id.* at 33 (stating that the “amount of Sr breakthrough activity must be strictly limited to the Health Canada guidelines”).

The dose calibrator “is utilized in the system for both calibration and testing” and “is used to detect the breakthrough activity as part of the calibration test through measurement of ^{82}Rb activity.” *Id.* at 19, 23, 50. Klein’s system is calibrated “by monitoring an external dose calibrator during the calibration run” (*id.* at 17) and “[w]ait[s] for decay to read breakthrough from dose calibrator” (*id.* at 64). The “dose calibrator is used to detect the breakthrough activity . . . through measurement of ^{82}Rb activity” and the “breakthrough of each isotope, $A_{82\text{Sr}}/A_{82\text{Rb}}$ and $A_{85\text{Sr}}/A_{82\text{Rb}}$, is calculated as a relative activity ratio of Sr activity to ^{82}Rb activity delivered.” *Id.* at 50–51.

Klein also describes a daily protocol “intended for routine system maintenance, system diagnostics, and clinical preparation of the system,” which includes a calibration run. *Id.* at 17–18. Klein states that “[o]nly after a calibration run with low Sr breakthrough has been successfully completed can patient elutions be carried out,” and “[o]nce the daily protocol has been completed successfully, patient elutions are enabled until the end of the day.” *Id.* at 18; *see also id.* at 33 (stating that the “issue is addressed by daily breakthrough tests as part of the daily protocol ensured by the system”), 43 (stating that “certain maintenance measures must be carried out as dictated by the daily protocol” and “Sr breakthrough must be measured

and a complete system test must follow”), 50–52 (describing breakthrough measurement), 122 (stating “[d]aily calibration samples are used to test for the breakthrough of Sr activity; if significant Sr activity is detected, the generator cannot be used on humans”). Klein also states that the “⁸²Rb infusion system software must ensure that the protocol is followed (i.e. that each run is enabled only after the prerequisites have been completed successfully).” *Id.* at 44.

2. *Independent Claim 1*

- a. “A system comprising: a shielding assembly configured to contain a radioisotope generator that generates radioactive eluate via elution”

Petitioner argues that Klein discloses a “system” and “a shielding assembly configured to contain a radioisotope generator that generates radioactive eluate via elution.” Pet. 23–25 (citing Ex. 1014, 1, 8, 19, 23–24; Ex. 1015 ¶¶ 199–210). Petitioner relies in part on annotated versions of Klein’s Figures 2-2 and 2-3, and points to a schematic of Klein’s elution system, as well as the shielded generator and shielded waste container carried on a cart. *Id.* at 24 (citing Ex. 1014, 19 (Fig. 2-2), 24 (Fig. 2-3)).

We find that Klein describes an “infusion system . . . based on a ⁸²Sr/⁸²Rb generator, which produces ⁸²Rb activity continuously.” Ex. 1014, 1. We also find that Klein shows a “Shielded Activity Counter” (Fig. 2-4), “Shielded Waste Container” (Fig. 2-3), and “Shielded Generator” (Fig. 2-3) on a stainless steel cart, and that “⁸²Rb is eluted in the form of ⁸²RbCl (eluate)” from the generator (*id.* at 8). *See also id.* at 23 (“All the components are assembled in a stainless steel cart shown in Figure 2-3.”), 24 (Figs. 2-3, 2-4), 36. We further credit Petitioner’s declarant testimony because Klein supports that testimony. Ex. 1015 ¶¶ 199–210 (citing

Ex. 1014, 1, 8, 19 (Fig. 2-2), 23–24 (Figs. 2-3, 2-4), 36, 46 (Fig. 3-6)).

Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose any of these limitations. See PO Resp. 8–19.

Based on the full record, because Klein discloses an infusion system that includes a shielded $^{82}\text{Sr}/^{82}\text{Rb}$ generator on a stainless steel cart that generates eluate, Petitioner persuades us by a preponderance of the evidence that Klein discloses a “system comprising: a shielding assembly configured to contain a radioisotope generator that generates radioactive eluate via elution.”

- b. *“a computer carried by the shielding assembly wherein the computer is configured to receive a user input and, responsive to receiving the user input, control the radioisotope generator to generate a sample of eluate via elution during breakthrough testing”*

Petitioner argues that Klein discloses a “a computer carried by the shielding assembly, wherein the computer is configured to receive a user input and, responsive to receiving the user input, control the radioisotope generator to generate a sample of eluate via elution during breakthrough testing.” Pet. 25–28 (citing Ex. 1014, 19, 20, 23–25, 30, 53–55; Ex. 1015 ¶¶ 211–221). Petitioner relies in part on annotated versions of Klein’s Figures 2-2 and 2-3, and points to Klein’s personal computer and LCD touch screen, as well as one of the input screens shown to the operator during operation of the system. *Id.* at 27 (citing Ex. 1014, 24 (Fig. 2-3), 54 (Fig. 3-12)).

We find that the relied-upon portions of Klein disclose a computer carried on a stainless steel cart, with the computer configured to receive user input via an LCD touch screen. Ex. 1014, 23, 25, 54. We also find that

Klein describes “allow[ing] the operator to control all the features of the elution system,” including operation of the generator to generate eluate via elution. *Id.* at 30, 53 (referring to steps taken by user to initiate the elution), 54 (showing screen prompts for use by operator in Fig. 3-12, including “Choose Run Type” in Fig. 3-12(c)), 55 (referring to “calibration (including a test of breakthrough activity) at the start of each day”). We further credit Petitioner’s declarant testimony because Klein supports that testimony. Ex. 1015 ¶¶ 211–221 (citing Ex. 1014, 19, 20, 23–25, 30, 53–55). Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose any of these limitations. *See* PO Resp. 8–19.

Based on the full record, because Klein discloses a computer and user input device carried on a cart containing shielding, as well as a series of operator inputs for controlling the elution system, Petitioner persuades us by a preponderance of the evidence that Klein discloses “a computer carried by the shielding assembly wherein the computer is configured to receive a user input and, responsive to receiving the user input, control the radioisotope generator to generate a sample of eluate via elution during breakthrough testing.”

c. *“a dose calibrator electronically coupled to the computer and configured to measure an activity of the sample of eluate generated during breakthrough testing”*

Petitioner argues that Klein discloses “a dose calibrator electronically coupled to the computer and configured to measure an activity of the sample of eluate generated during breakthrough testing.” Pet. 28–30 (citing Ex. 1014, 19, 23–24, 50; Ex. 1015 ¶¶ 222–227). Petitioner relies in part on annotated versions of Klein’s Figures 2-2 and 2-3, a schematic of Klein’s

system showing the dose calibrator and computer, as well a photo of Klein's dose calibrator ionization chamber and interface positioned next to Klein's cart. *Id.* at 29 (citing Ex. 1014, 19 (Fig. 2-2), 24 (Fig. 2-3)).

We find that the relied-upon portions of Klein disclose a dose calibrator connected to a computer. Ex. 1014, 19 (describing system with PC interfacing with components, and system acquiring data from dose calibrator), 24, Fig. 2-2 (depicting wired connection between dose calibrator and computer). We also find that Klein describes using the dose calibrator to test samples during breakthrough testing. *Id.* at 23, 50. We further credit Petitioner's declarant testimony because Klein supports that testimony. Ex. 1015 ¶¶ 222–227 (citing Ex. 1014, 19, 23–24, 50). Patent Owner does not address these limitations or Petitioner's related arguments and evidence, or argue that Klein fails to disclose any of these limitations. See PO Resp. 8–19.

Based on the full record, because Klein discloses a dose calibrator coupled to a computer and the dose calibrator measures a sample during breakthrough testing, Petitioner persuades us by a preponderance of the evidence that Klein discloses “a dose calibrator electronically coupled to the computer and configured to measure an activity of the sample of eluate generated during breakthrough testing.”

d. “wherein the computer carried by the shielding assembly is configured to receive the activity data from the dose calibrator and calculate breakthrough test results”

Petitioner argues that Klein discloses “wherein the computer carried by the shielding assembly is configured to receive the activity data from the dose calibrator and calculate breakthrough test results.” Pet. 30–31 (citing Ex. 1014, 17, 19, 50–51, 64; Ex. 1015 ¶¶ 228–239). Petitioner relies in part

on an annotated version of Klein’s Figure 2-2, a schematic of Klein’s system showing the dose calibrator and computer. *Id.* at 30 (citing Ex. 1014, 19 (Fig. 2-2)).

As discussed above, we find that Klein discloses a computer carried by a shielded assembly. We also find that Klein discloses a computer that receives activity data from its dose calibrator. Ex. 1014, 19 (describing system with PC interfacing with components, and system acquiring data from dose calibrator), 24, Fig. 2-2 (depicting wired connection between dose calibrator and computer). Klein also describes using the dose calibrator to calculate breakthrough test results. *Id.* at 50–51 (“The breakthrough of each isotope . . . is calculated”). We further credit Petitioner’s declarant testimony because Klein supports that testimony. Ex. 1015 ¶¶ 228–239 (citing Ex. 1014, 17, 19, 50–51, 55, 64). Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose any of these limitations. *See* PO Resp. 8–19.

Based on the full record, because Klein discloses a dose calibrator coupled to a computer, where the computer calculates breakthrough test results, Petitioner persuades us by a preponderance of the evidence that Klein discloses “wherein the computer carried by the shielding assembly is configured to receive the activity data from the dose calibrator and calculate breakthrough test results.”

- e. *“the computer is further configured to prevent a patient infusion procedure if a breakthrough test result exceeds an allowable limit”*

(1) Parties’ Positions

Petitioner argues that Klein discloses “the computer is further configured to prevent a patient infusion procedure if a breakthrough test

result exceeds an allowable limit.” Pet. 32–33 (citing Ex. 1014, 18, 19, 29, 33, 44, 55, 122; Ex. 1015 ¶¶ 240–249). Petitioner relies in part on portions of Klein emphasizing software control of the system and the importance of following a daily protocol that requires a successful breakthrough test measurement before any elutions can be performed on patients. *See id.*

Patent Owner responds that Klein does not disclose expressly a computer that prevents patient infusions if a breakthrough test result exceeds an allowable limit. PO Resp. 1, 8, 12–19. Patent Owner notes that Petitioner’s arguments and evidence that Klein’s computer prevents infusion if breakthrough test results exceed an allowable limit are the same in this proceeding and the related proceedings, IPR2018-01448 and IPR2018-01450. *Id.* at 9–11.

According to Patent Owner, Petitioner implicitly acknowledges that Klein does not expressly state that a computer prevents infusions if breakthrough test results exceed an allowable limit, and the relied-upon portions of Klein fail to disclose expressly such a computer. *Id.* at 12–13 (citing Pet. 23, 32–33, 47–48⁶; Ex. 1015 ¶¶ 166, 248, 343). Also, according to Patent Owner, although Klein resets at midnight and prohibits infusions until a daily protocol is completed, the computer of Klein does not prevent infusions if breakthrough test results exceed an allowable limit, because the “decision is left to the operator.” *Id.* at 13 (citing Ex. 2003 ¶¶ 95–96).

Patent Owner contends that Klein’s computer merely “facilitates testing for strontium breakthrough.” *Id.* (citing Ex. 1014, 53–55). In Patent

⁶ We view Patent Owner’s citation to pages “47–28” as a typographical error. PO Resp. 12. Pages 47–48 correspond to the relevant portions of the analysis of claim 13 in the Petition.

Owner's view, Klein describes an experiment for observing excessive breakthrough, and the experiment would have been complicated or impossible if Klein's computer prevented infusions based on breakthrough testing. *Id.* at 14 (citing Ex. 1014, 122; Ex. 2003 ¶ 97). Patent Owner also argues that Klein does not describe its computer preventing infusions or having to override the system after breakthrough was observed, and thus, one of ordinary skill in the art would have understood that an operator must prevent infusions if breakthrough is detected. *Id.*

Patent Owner further argues that (1) Klein discloses an operator may manually enter breakthrough activity from a more sensitive instrument, (2) Klein does not state clearly that the system is locked out until breakthrough activity is entered, (3) Klein lists error messages, none of which pertain to locking out based on breakthrough testing, and (4) Klein discloses that automatic testing of activity can fail so that the system could not determine breakthrough and may not be locked out. *Id.* at 14–15 (citing Ex. 1014, 52, 54, 61, Fig. 3-12; Ex. 2003 ¶¶ 98–99). Patent Owner also directs us to its declarant's testimony in the related ITC proceeding. *Id.* at 15–16 (citing Ex. 2012, 983:10–984:23). Further, based on Figure 3-15 of Klein, which includes the step "Wait for Breakthrough Reading," Patent Owner argues that the daily protocol is satisfied merely if Klein's system can acquire data from the dose calibrator. *Id.* at 16–18 (citing Ex. 1014, Fig. 3-15; Ex. 2003 ¶¶ 100–101; Ex. 2003, 981:22–983:9). Patent Owner asserts that Petitioner is also relying on express anticipation, not inherent anticipation. *Id.* at 18.

Petitioner replies that Klein discloses a computer-controlled infusion system with disabled touchscreen buttons that "disables Patient Elution Runs

each night,” and Patent Owner’s declarant agrees. Pet. Reply 3–6 (citing Ex. 1014, 17–19, 29–31, 44, 53–54, Fig. 3-12(c); Ex. 1015 ¶¶ 143–153, 157–166; Ex. 2012, 981:9–10, 1078:8–1079:12). Petitioner also replies that anticipation “does not demand word-for-word correspondence between prior art and the claims” and that one of ordinary skill in the art would “recognize immediately from Klein’s disclosure that the computer ‘prevent[s] the patient infusion procedure if a breakthrough test result exceeds an allowable limit.’” *Id.* at 7.

Regarding Patent Owner’s arguments that Klein’s breakthrough experiments suggest that its computer does not prevent infusions, Petitioner replies that those experiments were not patient infusion procedures, Klein distinguishes the experiments from patient procedures, Klein never suggests that those experiments involved patient procedures, and Klein prevents patient infusion procedures as claimed. *Id.* at 7–9 (citing PO Resp. 14–15; Ex. 1014, 53, 122, Fig. 3-15; Ex. 1015 ¶¶ 240–249, 335–344). Petitioner argues that the claims do not require that the computer disable all operation, only patient infusion procedures. *Id.* at 9.

Regarding Patent Owner’s argument based on Klein’s manual entry of breakthrough results, Petitioner replies that Klein teaches that manual entry is not normally done, manual entry would still be consistent with Klein’s computer performing lockout, manual entry of breakthrough measurements would also ensure that the daily protocol is followed, and “automated breakthrough testing suffices in many cases,” thus operating as required by claim 1. *Id.* at 9–10 (citing Ex. 1014, 43, 64).

Petitioner also argues that Patent Owner’s declarant testimony that a calibration run would be successful even if high strontium breakthrough

levels were detected is inconsistent with a plain reading of Klein and not credible. *Id.* at 10–11 (citing PO Resp. 16–18; Ex. 1014, Fig. 3-15; Ex. 2012, 981:22–983:9). Petitioner further argues that Klein’s breakthrough tests are completed successfully “only when test results show low strontium breakthrough.” *Id.* at 11 (citing Ex. 1014, 18). Petitioner argues that Klein’s software, not the operator, enables patient elution runs because Klein’s computer disables elutions each night and re-enables elutions only after breakthrough test results meet allowable limits. *Id.* (citing Ex. 1014, 29, 33, 44).

Patent Owner replies that “Petitioner’s case is predicated on reading into Klein something that does not exist – an express disclosure of the computer preventing patient infusions based on strontium breakthrough test results” and “rel[ies] on piecemeal quotations from Klein.” PO Sur-Reply 1 (citing Pet. Reply 6); *see also id.* at 2 (arguing that Petitioner “relies on selectively excerpting the record and mere attorney argument”). Patent Owner also argues that its declarant provided testimony in the ITC proceeding regarding Klein’s breakthrough testing and that the testimony is unchallenged. *Id.* at 1–3 (citing Ex. 2012, 971:4–19, 1078:21–23).

Patent Owner contends that Klein does not disclose a computer preventing patient infusion if breakthrough test results exceed an allowable limit and “Petitioner conflates the issues by pointing to disclosures in Klein relating to whether/when the system is locked out due to expiration of system calibration, not due to breakthrough results exceeding an allowable limit.” *Id.* at 3 (citing PO Resp. 13–20; Pet. Reply 3–11). According to Patent Owner, Petitioner incorrectly contends that Patent Owner’s declarant agreed that Klein’s system is locked out until breakthrough testing is

performed. *Id.* at 3–4 (citing Pet. Reply 5). Patent Owner argues that its declarant testimony is consistent with the portions of Klein relied upon by Petitioner. *Id.* at 4 (citing Pet. Reply 5–6; Ex. 1014, 17; Ex. 2012, 983:7–9, 982:25–983:6).

Patent Owner also argues that Petitioner misreads Klein’s statement that “[o]nly after a calibration run with low Sr breakthrough has been successfully completed can patient elutions be carried out” and Petitioner selectively quotes Klein. *Id.* at 4 (citing Pet. Reply 11; Ex. 1014, 18). Patent Owner asserts that none of the relied-upon portions of Klein expressly discloses a computer preventing infusion procedures based on breakthrough testing results. *Id.* at 4–5 (citing Pet. Reply 11; Ex. 1014, 44; Ex. 2003 ¶ 95). Patent Owner states that “there is no question that Klein requires that the calibration protocol is followed” but “Klein does not disclose that the computer prevents patient infusions if a strontium breakthrough test result exceeds an allowable limit.” *Id.* at 5 (citing Ex. 1014, 44).

Patent Owner further replies that Petitioner did not depose Patent Owner’s declarant Dr. Pelc and relies on attorney arguments to contend that one of ordinary skill in the art would understand Klein discloses a computer preventing infusion procedures. *Id.* at 5–6 (citing Pet. Reply 6, 7). Patent Owner also argues that Petitioner implicitly admits that Klein does not disclose such a computer because Petitioner relies on declarant testimony. *Id.* at 6 (citing Pet. Reply 7; Ex. 1015 ¶ 252). Patent Owner likens Klein’s disclosures to the Bracco Manual, which does not disclose a computer performing breakthrough testing or preventing patient infusions. *Id.* at 6–7 (citing Ex. 1021, 31, 34–35). Patent Owner, thus, contends that Klein does not disclose a computer preventing infusions, as contended by Petitioner, but

instead “teaches that the decision to perform patient infusions based on a strontium breakthrough test result is left to the operator.” *Id.* at 7 (citing Pet. Reply 5; Ex. 2003 ¶¶ 95–96).

Patent Owner also points to Klein’s statement that “[i]f the eluted ⁸²Rb activity is insufficient to accurately measure breakthrough, the automatic measurement is skipped,” and argues that one of ordinary skill in the art would not have understood Klein to be disclosing that its computer prevents patient elutions when skipping the automatic measurement, or a requirement for manual entry when the skipping occurs. *Id.* at 7 (citing Pet. Reply 9; Ex. 1014, 52; Ex. 2012, 983:10–984:23).

Regarding Petitioner’s argument that “if significant Sr activity is detected, ***the generator cannot be used on humans***,” Patent Owner contends that “Klein does not mention the computer preventing a patient infusion due to such significant Sr activity” but Klein supports Patent Owner’s declarant’s analysis that “the operator, not the computer, makes the decision.” *Id.* at 8 (citing Pet. Reply 9; Ex. 2003 ¶ 97).

(2) Whether Klein Discloses a Computer Preventing a Patient Infusion Procedure if a Breakthrough Test Result Exceeds an Allowable Limit

We find that Petitioner’s relied-upon portions of Klein disclose that (1) “[o]nce the daily protocol has been completed successfully, patient elutions are enabled until the end of the day” (Ex. 1014, 18); (2) the “amount of Sr breakthrough activity must be strictly limited to the Health Canada guidelines” (*id.* at 33); (3) “[t]his issue is addressed by daily breakthrough tests as part of the daily protocol ensured by the system” (*id.*); (4) the “⁸²Rb infusion system software must ensure that the protocol is followed (i.e. that each run is enabled only after the prerequisites have been completed

successfully)” (*id.* at 44); (5) “it ensures that the daily protocol is followed, including a flush and calibration (including a test of breakthrough activity) at the start of each day” (*id.* at 55); and (6) “[d]aily calibration samples are used to test for the breakthrough of Sr activity; if significant Sr activity is detected, the generator cannot be used on humans” (*id.* at 122). *See also* Pet. 32–33 (citing Ex. 1014, 18, 19, 29, 33, 44, 55, 122; Ex. 1015 ¶¶ 143–153, 157–166, 240–249).

We, thus, find that, because Klein’s software ensures the daily protocol is followed and patient elutions or runs are “**enabled**” once the daily protocol is completed successfully, one of ordinary skill in the art would have understood that Klein discloses a computer that is configured via software to prevent or not enable patient infusion if the daily protocol is not completed successfully. *See also* Ex. 1014, 17–18 (describing that the “protocol consists of a system flush and a calibration run” and that “[a]lthough the outline remains unchanged, the protocol was slightly modified to remove operator intervention where automation was introduced”).

As for breakthrough testing, Klein expressly discloses that “Sr breakthrough . . . is tested for on a daily basis as part of the daily protocol” (Ex. 1014, 122), the “amount of Sr breakthrough activity must be strictly limited to the Health Canada guidelines” (*id.* at 33), and “[t]his issue is addressed by daily breakthrough tests as part of the daily protocol ensured by the system” (*id.*). We, thus, find that one of ordinary skill in the art would have understood that Klein discloses breakthrough testing is part of the daily protocol that must be completed successfully to enable patient elutions.

We also find that a relied-upon portion of Klein discloses that “[d]aily calibration samples are used to test for the breakthrough of Sr activity” and “if significant Sr activity is detected, the generator cannot be used on humans.” *Id.* at 122. As discussed above, we find that Klein discloses that it calculates ^{82}Sr and ^{85}Sr activities relative to ^{82}Rb activity during breakthrough testing. Thus, Klein expressly discloses that “if a breakthrough test result exceeds an allowable limit,” that is, if significant Sr activity indicating breakthrough is detected, then the generator should not be used and, therefore, a patient infusion procedure will not be enabled.

Based on the full record, because Klein discloses software that ensures the daily protocol, which includes breakthrough testing, is followed, and patient elutions are enabled only if the daily protocol is completed successfully, Petitioner persuades us by a preponderance of the evidence that Klein discloses “the computer is further configured to prevent a patient infusion procedure if a breakthrough test result exceeds an allowable limit.”⁷

Turning to Patent Owner’s argument that an operator prevents infusions if breakthrough is detected, Petitioner persuades us that Klein’s

⁷ Although the parties did not present or brief a broader interpretation, these limitations could be interpreted more broadly than implied by the parties’ arguments. For example, the limitation at issue does not exclude any and all operator intervention because a computer can still be configured to prevent a procedure even if additional operator action is required. *See* Tr. 19:15–20:16 (Petitioner’s counsel answering questions about possible broader interpretation), 48:19–49:15 (Patent Owner’s counsel answering questions about possible broader interpretation). For our analysis, because the parties dispute whether Klein’s computer, standing alone, prevents a procedure without operator intervention if breakthrough test results exceed an allowable limit, we have applied the parties’ implied, narrower interpretation.

software, not an operator, enables patient infusions only if the daily protocol, which includes breakthrough testing, is completed successfully. Also, Klein's disclosures of manually entering breakthrough activity from a more sensitive instrument if such activity is not available from the dose calibrator, and Klein's description of a breakthrough experiment, do not address whether operator intervention is required when readings are available from the dose calibrator and when there is no breakthrough experiment.

During oral hearing, Patent Owner's counsel argued that independent claim 21 of U.S. Patent No. 9,299,468 B2, at issue in the related IPR proceedings, recites four steps of measuring activity, calculating a strontium activity, comparing a strontium activity to an allowable limit, and preventing infusion if the strontium activity exceeds the limit. Tr. 47:4–48:18, 49:16–20, 73:17–20. Patent Owner's counsel contended that Klein discloses a computer that performs the first step, automatically measuring activity, but not the other three steps. *See, e.g., id.* at 48:6–18, 58:8–16, 59:16–60:5, 60:14–61:17, 70:23–71:3. Petitioner's counsel objected to these arguments because they were not the arguments previously presented. *See id.* at 73:17–20, 95:14–96:3.

We agree with Petitioner that Patent Owner did not assert explicitly in its authorized briefing that any of the challenges claims require four steps, only one of which is completed automatically. Further, Patent Owner did not explain adequately how its analysis at the hearing ties into claim 1 (or any claim) of the '467 patent at issue here. We view these arguments as beyond the scope of Patent Owner's arguments in its briefing in this case, and thus, determine that these arguments were waived. To the extent that these arguments could be said to be within the scope of what was previously

presented, we determine them to be unpersuasive, because Klein discloses software that ensures the daily protocol, which includes breakthrough testing, is followed and patient elutions are enabled only if the daily protocol is completed successfully. Thus, Petitioner persuades us by a preponderance of the evidence that one of ordinary skill in the art would have understood that Klein discloses a computer that measures activity, calculates breakthrough test results, compares those test results to an allowable limit, and prevents infusion if the breakthrough test result exceeds the limit.

3. Independent Claim 13

Independent claim 13 contains limitations similar to those in claim 1. With the exception of the step requiring “preventing, . . . a patient infusion procedure if a breakthrough test result exceeds an allowable limit,” Patent Owner does not address Petitioner’s arguments and evidence as to claim 13. *See* PO Resp. 8–19.

a. “A method comprising: generating, with a radioisotope generator contained within a shielding assembly, a radioactive eluate via elution of an eluant”

Petitioner argues that Klein discloses a method that includes the step of “generating, with a radioisotope generator contained within a shielding assembly, a radioactive eluate via elution of an eluant.” Pet. 42–45 (citing Ex. 1014, 1, 8, 19, 23–24; Ex. 1015 ¶¶ 311–319). Petitioner relies in part on annotated versions of Klein’s Figures 2-2 and 2-3, and points to a schematic of Klein’s elution system, as well as a photo of the shielded generator and shielded waste container carried on a cart. *Id.* at 43 (citing Ex. 1014, 19 (Fig. 2-2), 24 (Fig. 2-3)).

We find that Klein describes an “infusion system . . . based on a $^{82}\text{Sr}/^{82}\text{Rb}$ generator, which produces ^{82}Rb activity continuously.” Ex. 1014,

1. We also find that Klein shows a “Shielded Activity Counter” (Fig. 2-4), “Shielded Waste Container” (Fig. 2-3), and “Shielded Generator” (Fig. 2-3) on a stainless steel cart, and that “ ^{82}Rb is eluted in the form of $^{82}\text{RbCl}$ (eluate)” from the generator (*id.* at 8). *See also id.* at 23 (“All the components are assembled in a stainless steel cart shown in Figure 2-3.”), 24 (Figs. 2-3, 2-4), 36. We further credit Petitioner’s declarant testimony because Klein supports that testimony. Ex. 1015 ¶¶ 311–319 (citing Ex. 1014, 1, 8, 19 (Fig. 2-2), 23–24 (Figs. 2-3, 2-4)). Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose any of these limitations. *See* PO Resp. 8–19.

Based on the full record, because Klein discloses a method that includes generating eluate using a shielded $^{82}\text{Sr}/^{82}\text{Rb}$ generator on a stainless steel cart, Petitioner persuades us by a preponderance of the evidence that Klein discloses a “method comprising: generating, with a radioisotope generator contained within a shielding assembly, a radioactive eluate via elution of an eluant.”

b. *“measuring, with a dose calibrator electronically coupled to a computer carried by the shielding assembly, an activity of the radioactive eluate”*

Petitioner argues that Klein discloses a method that includes the step of “measuring, with a dose calibrator electronically coupled to a computer carried by the shielding assembly, an activity of the radioactive eluate.” Pet. 44–46 (citing Ex. 1014, 19, 23, 50; Ex. 1015 ¶¶ 320–329). Petitioner relies in part on annotated versions of Klein’s Figures 2-2 and 2-3. *Id.* at 44 (citing Ex. 1014, 19 (Fig. 2-2), 24 (Fig. 2-3)).

We find that the relied-upon portions of Klein disclose a dose calibrator connected to a computer carried by a shielded assembly, as discussed above. Ex. 1014, 19 (describing system with PC interfacing with components, and system acquiring data from dose calibrator), 23, 24, Fig. 2-2 (depicting wired connection between dose calibrator and computer). We also find that Klein describes using the dose calibrator to measure the activity of test samples during breakthrough testing. *Id.* at 23, 50. We further credit Petitioner’s declarant testimony because Klein supports that testimony. Ex. 1015 ¶¶ 320–329 (citing Ex. 1014, 19, 23–25, 50). Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose any of these limitations. *See* PO Resp. 8–19.

Based on the full record, because Klein discloses a method that includes measuring activity of an eluate using a shielded $^{82}\text{Sr}/^{82}\text{Rb}$ generator on a stainless steel cart, Petitioner persuades us by a preponderance of the evidence that Klein discloses a “measuring, with a dose calibrator electronically coupled to a computer carried by the shielding assembly, an activity of the radioactive eluate.”

c. *“determining, with the computer, an activity of rubidium-82 within the radioactive eluate”*

Petitioner argues that Klein discloses a method that includes the step of “determining, with the computer, an activity of rubidium-82 within the radioactive eluate.” Pet. 46–47 (citing Ex. 1014, 50–51; Ex. 1015 ¶¶ 330–334). Petitioner relies in part on an annotated version of Klein’s Figure 2-3. *Id.* at 46 (citing Ex. 1014, 24 (Fig. 2-3)).

We find that the relied-upon portions of Klein disclose a computer that determines the activity of rubidium-82 with an eluate. Ex. 1014, 51

(describing calculation of rubidium-82 activity). We further credit Petitioner’s declarant testimony because Klein supports that testimony. Ex. 1015 ¶¶ 330–334 (citing Ex. 1014, 24, 50–51). Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose any of these limitations. See PO Resp. 8–19.

Based on the full record, because Klein discloses a method that includes determining rubidium-82 activity within an eluate, Petitioner persuades us by a preponderance of the evidence that Klein discloses a “determining, with the computer, an activity of rubidium-82 within the radioactive eluate.”

d. “preventing, with the computer, a patient infusion procedure if a breakthrough test result exceeds an allowable limit”

Petitioner argues that Klein discloses a method that includes the step of “preventing, with the computer, a patient infusion procedure if a breakthrough test result exceeds an allowable limit.” Pet. 47–48 (citing Ex. 1014, 18, 29, 33, 44, 50, 122; Ex. 1015 ¶¶ 335–344). Petitioner relies in part on portions of Klein emphasizing software control of the system and the importance of following a daily protocol that requires a successful breakthrough test measurement before any elutions can be performed on patients. See *id.*

Patent Owner argues that Klein does not disclose the “preventing” step of claim 13 for the same reasons that Klein fails to disclose the “prevent a patient infusion” limitation in claim 1. See PO Resp. 1, 8, 12–19 (arguing these limitations in claims 1 and 13 together); Pet. Reply 2–11 (arguing the similar limitations in claims 1 and 13 together). For the reasons discussed above, we find Patent Owner’s arguments unconvincing, as we are

persuaded by Petitioner’s arguments and evidence that Klein discloses the use of a computer to prevent infusions if breakthrough tests exceed an allowable limit. *See, supra*, § III.D.2.e.

As discussed above, based on the full record, because Klein discloses software that ensures the daily protocol, which includes breakthrough testing, is followed, and patient elutions are enabled only if the daily protocol is completed successfully, Petitioner persuades us by a preponderance of the evidence that Klein discloses “preventing, with the computer, a patient infusion procedure if a breakthrough test result exceeds an allowable limit.”

4. *Dependent Claim 2*

Claim 2 depends from claim 1 and recites “wherein the radioisotope generator comprises a strontium-rubidium generator configured to generate rubidium-82 by decay of strontium-82.” Ex. 1001, 23:65–67. Petitioner argues that Klein discloses this limitation. Pet. 33–34 (citing Ex. 1014, 8, 19; Ex. 1015 ¶¶ 250–255).

We find that the relied-upon portions of Klein teach that the “⁸²Rb can be supplied using a ⁸²Sr/⁸²Rb generator. . . . The generator must be loaded roughly every two months with Strontium-82.” Ex. 1014, 8. We also find that Klein discloses that, in its system, strontium “decays to” rubidium. *Id.*; *see also id.* at 19, Fig. 2-2 (showing “⁸²Sr/⁸²Rb Generator” in schematic of Klein’s system). We further credit Petitioner’s declarant testimony because the relied-upon portions of Klein support that testimony. Ex. 1015 ¶¶ 250–255 (citing Ex. 1014, 8, 19). Patent Owner does not address this limitation or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose this limitation. *See* PO Resp. 8–19.

Because Klein discloses a strontium-rubidium generator supplied with strontium to supply rubidium, Petitioner persuades us by a preponderance of the evidence that Klein discloses “wherein the radioisotope generator comprises a strontium-rubidium generator configured to generate rubidium-82 by decay of strontium-82.”

5. Dependent Claims 3 and 4

Claim 3 depends from claim 1 and recites “wherein the computer is configured to calculate the breakthrough test results by at least calculating a ratio of an activity of strontium-82 divided by an activity of rubidium-82 and a ratio of an activity of strontium-85 divided by the activity of rubidium-82.” Ex. 1001, 24:1–5. Claim 4 depends from claim 3 and further requires “wherein the computer is further configured to indicate if the breakthrough test results are within allowable limits.” *Id.* at 24:6–8. Petitioner argues that Klein discloses these limitations. Pet. 34–37 (citing Ex. 1014, 9, 18, 24, 29, 33, 51, 122; Ex. 1015 ¶¶ 256–273).

We find that the relied-upon portions of Klein disclose that breakthrough tests are calculated, in part, by calculating the ratio of the activity of strontium-82 to rubidium-82 and the ratio of the activity of strontium-85 to rubidium-82. Ex. 1014, 51. We also find that Klein discloses a computer that indicates if the breakthrough test results are within allowable limits. *Id.* at 18 29, 33, 122 (“Daily calibration samples are used to test for the breakthrough of Sr activity; if significant Sr activity is detected, the generator cannot be used on humans.”). We further credit Petitioner’s declarant testimony because the relied-upon portions of Klein support that testimony. Ex. 1015 ¶¶ 250–255 (citing Ex. 1014, 9, 18, 24, 29, 33, 51, 122). Patent Owner does not address these limitations or Petitioner’s

related arguments and evidence, or argue that Klein fails to disclose any of these limitations. *See* PO Resp. 8–19.

Because Klein discloses calculating breakthrough test results using the ratios claimed in claim 3 and indicates whether the test results are within allowable limits as required by claim 4, Petitioner persuades us by a preponderance of the evidence that Klein discloses the limitations of claims 3 and 4.

6. Dependent Claims 6, 7, 19, and 20

Claim 6 depends from claim 1 and recites “an activity detector.” Ex. 1001, 24:15–16. Claim 7 depends from claim 6 and further requires “wherein the computer is configured to divert eluate generated via elution to a waste bottle until the activity detector detects a given level of activity.” *Id.* at 24:17–19. Claims 19 and 20 also address an activity detector and diversion of eluate. Claim 19 depends from claim 13 and recites “measuring, with an activity detector electronically coupled to the computer, an activity of the radioactive eluate.” *Id.* at 24:65–67. Claim 20 depends from claim 19 and further requires “controlling, with the computer, a diverter valve to divert the radioactive eluate to a waste bottle until the activity detector detects a given level of activity.” *Id.* at 25:1–4. Petitioner argues that Klein discloses these limitations. Pet. 37–39, 53–55 (citing Ex. 1014, 19, 24, 41, 44–45, 52, 58; Ex. 1015 ¶¶ 274–285, 376–382).

We find that the relied-upon portions of Klein disclose an activity detector connected to a computer that measures the activity of the radioactive eluate. Ex. 1014, 19 (describing PC interfacing with activity counter and Fig. 2-2 showing “Activity Counter” connected to computer), 52. We also find that Klein discloses a “Patient Valve” that switches flow

from a waste container to a patient outlet once a “threshold activity” is reached. *Id.* at 44–45. We further credit Petitioner’s declarant testimony because the relied-upon portions of Klein support that testimony. Ex. 1015 ¶¶ 274–285, 376–382 (citing Ex. 1014, 19, 24, 41, 44–45, 52, 58). Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose any of these limitations. *See* PO Resp. 8–19.

Because Klein discloses an activity counter connected to a computer that measures the activity level of the eluate, and a valve used to divert eluate from a waste container to a patient outlet only after a certain activity is reached, Petitioner persuades us by a preponderance of the evidence that Klein discloses the limitations of claims 6, 7, 19, and 20.

7. Dependent Claims 9, 10, and 18

Claim 9 depends from claim 1 and recites “a display configured to display the breakthrough test results.” Ex. 1001, 24:22–23. Claim 10 depends from claim 9 and further requires “wherein the computer is configured to control the display to provide an indication of progress of the breakthrough testing.” *Id.* at 24:24–26. Claim 18 depends from claim 13 and, similarly to claim 9, recites “displaying breakthrough test results determined by the computer.” *Id.* at 24:63–64. Petitioner argues that Klein discloses these limitations. Pet. 39–41, 52–53 (citing Ex. 1014, 23, 24, 29, 31, 53, 56; Ex. 1015 ¶¶ 286–301, 366–375).

We find that the relied-upon portions of Klein disclose an LCD display that shows breakthrough test results determined by the computer. Ex. 1014, 24, Fig. 2-3 (depicting “LCD Touch Screen” and “Personal Computer”), 31 (describing display of statistics related to elution, which

would include breakthrough tests when those tests are performed). We also find that Klein discloses a “real-time graphics display” that includes current activity readings, and “progress bars . . . for each stage of the elution.” *Id.* at 31. We further credit Petitioner’s declarant testimony because the relied-upon portions of Klein support that testimony. Ex. 1015 ¶¶ 286–301, 366–375 (citing Ex. 1014, 23, 24, 29, 31, 53, 56). Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that Klein fails to disclose any of these limitations. See PO Resp. 8–19.

Because Klein discloses a display of breakthrough test results on a screen, including real-time progress results, and use of the computer and display in breakthrough testing, Petitioner persuades us by a preponderance of the evidence that Klein discloses the limitations of claims 9, 10, and 18.

8. Dependent Claim 12

Claim 12 depends from claim 1 and recites “wherein the dose calibrator is configured to physically receive the sample of eluate generated during breakthrough testing.” Ex. 1001, 24:31–33. Petitioner argues that Klein discloses this limitation. Pet. 41–42 (citing Ex. 1014, 24, 47, 50–51, 101; Ex. 1015 ¶¶ 304–309).

We find that the relied-upon portions of Klein disclose a dose calibrator that receives eluate generated during breakthrough testing. Ex. 1014, 24, Fig. 2-3 (depicting “Dose Calibrator” connected via lines to patient), 47, Fig. 3–7 (depicting “Patient Line” entering “Calibrator Chamber”). We further credit Petitioner’s declarant testimony because the relied-upon portions of Klein support that testimony. Ex. 1015 ¶¶ 302–309 (citing Ex. 1014, 24, 47, 50–51, 101). Patent Owner does not address this

limitation or Petitioner's related arguments and evidence, or argue that Klein fails to disclose this limitation. *See* PO Resp. 8–19.

Because Klein discloses a dose calibrator with a chamber that physically receives eluate from a patient via a line, Petitioner persuades us by a preponderance of the evidence that Klein discloses the limitation of claim 12.

9. Dependent Claims 14–16

Claim 14 depends from claim 13 and recites “determining, with the computer, an activity of strontium-82 and an activity of strontium-85 in the radioactive eluate.” Ex. 1001, 24:45–47. Claim 15 depends from claim 14 and further requires “determining, with the computer, a ratio of the activity of strontium-82 divided by the activity of rubidium-82 and a ratio of the activity of strontium-85 divided by the activity of rubidium-82.” *Id.* at 24:48–52. Claim 16 depends from claim 15 and recites “determining, with the computer, if the ratio of activity of strontium-82 divided by the activity of rubidium-82 and the ratio of the activity of strontium-85 divided by the activity of rubidium-82 are within allowable limits.” *Id.* at 24:53–57. Petitioner argues that Klein discloses these limitations. Pet. 49–52 (citing Ex. 1014, 24, 33, 50–52, 122; Ex. 1015 ¶¶ 347–365).

We find that the relied-upon portions of Klein disclose determining, with a computer, the activity levels of strontium-82 and -85, a ratio of the activity levels of strontium -82 to rubidium-82, and a ratio of the activity levels of strontium-85 to rubidium-82. Ex. 1014, 24 (showing use of computer), 50–51 (showing activity levels and ratios). We also find that Klein discloses determining if the activity level ratios are within allowable limits. *Id.* at 33, 50–51, 52 (showing allowable limits), 122. We further

credit Petitioner's declarant testimony because the relied-upon portions of Klein support that testimony. Ex. 1015 ¶¶ 347–365 (citing Ex. 1014, 24, 33, 50–52, 122). Patent Owner does not address these limitations or Petitioner's related arguments and evidence, or argue that Klein fails to disclose any of these limitations. See PO Resp. 8–19.

Because Klein discloses determining the claimed activity levels and ratios, and determining when the activity level ratios are within allowable limits, Petitioner persuades us by a preponderance of the evidence that Klein discloses the limitations of claims 14–16.

10. Conclusion as to Challenges Under 35 U.S.C. § 102

Based on the foregoing, Petitioner persuades us by a preponderance of the evidence that claims 1–4, 6, 7, 9, 10, 12–16, and 18–20 are unpatentable as anticipated by Klein.

E. Challenge Under 35 U.S.C. § 103 Based on Klein and Tate

Petitioner challenges dependent claims 11 and 22 as unpatentable as obvious based on Klein and Tate. Pet. 56–64. For these challenges, Petitioner cites to the asserted references and declarant testimony. *Id.* Patent Owner does not address Petitioner's challenge of claims 11 and 22. See generally PO Resp.; PO Sur-Reply.

We summarized the content of Klein above. We begin our analysis by summarizing Tate, then address Petitioner's arguments and evidence as to whether the Klein-Tate combination discloses the limitations of claim 11 and 22, and Petitioner's proffered reasons to combine the references.

1. *Tate (Ex. 1022)*

Tate “relates to methods, systems and components thereof for delivering pharmaceutical substances to patients for imaging procedures.”

Ex. 1022 ¶ 2. Figure 1E of Tate is reproduced below.

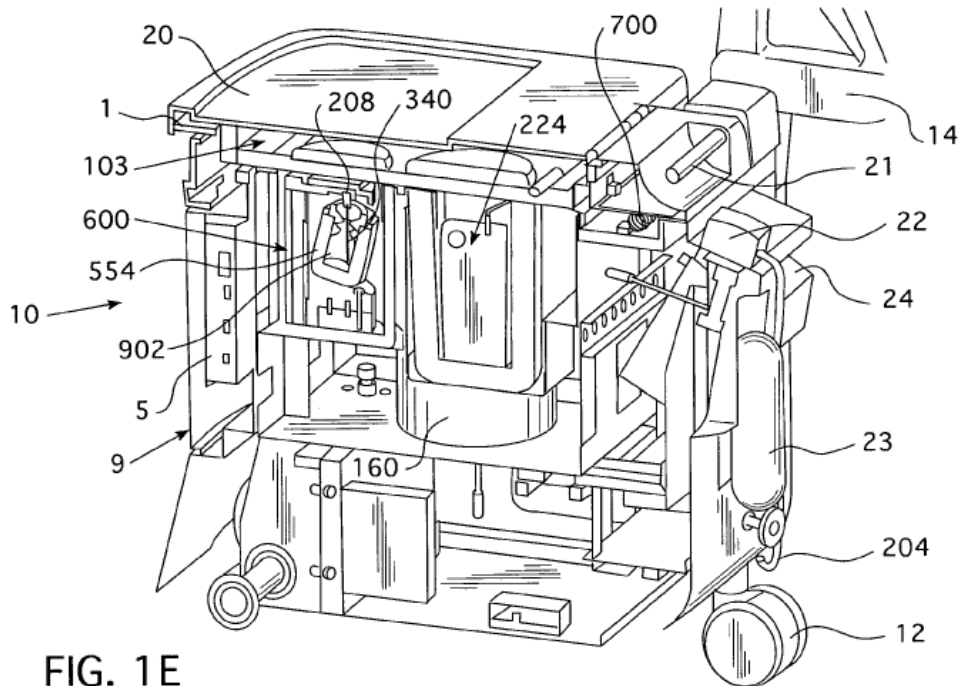


FIG. 1E

Figure 1E shows a cross-sectional view of a fluid delivery system. *Id.* ¶¶ 32, 36. Preferably, fluid delivery system 10 is a cart-like apparatus 9 and includes system controller 5 (preferably a single-board computer) that communicates with graphical user interface 15 (shown in Figure 1A), pumps, dose calibrator or ionization chamber 160, and other components. *Id.* ¶¶ 70, 84.

Fluid delivery system 10 also includes lid or cover 20, which preferably includes radioactive shielding to minimize radiation exposure from a radiopharmaceutical. *Id.* ¶¶ 72, 73; *see also id.* ¶¶ 9, 10, 87 (describing that long-term radiation exposure can pose a health risk, shielding personnel from a radiation source minimizes radiation exposure,

and recessed portions are preferably encased with suitable radioactive shielding to minimize exposure). Also, radiopharmaceutical vial or container 902 is in vial shield or FIG 554. *Id.* ¶ 79.

2. Dependent Claims 11 and 22

Claim 11 depends from claim 1 and recites “a cabinet structure, wherein the shielding assembly is positioned inside the cabinet structure and the computer is carried by the cabinet structure.” Ex. 1001, 24:27–30. Claim 22 depends from claim 13 and, similarly to claim 11, recites “wherein the shielding assembly is positioned inside a cabinet structure and the computer is carried by the cabinet structure.” *Id.* at 25:7–9. For claims 11 and 22, Petitioner argues that Klein discloses a shielding assembly that includes a stainless steel cabinet structure, but does not disclose a shielding assembly positioned *inside* the cabinet structure as required by these claims. Pet. 56. Petitioner argues that Tate discloses a cart structure for radioactive pharmaceuticals, and includes a cabinet structure, and a shielding assembly inside the cabinet structure, with a computer and a controller carried by the cabinet structure. *Id.* at 57. Petitioner provides a claim chart that indicates where Klein and Tate teach the limitations of claims 11 and 22, and the relevant support in Petitioner’s declarant testimony. *Id.* at 61–64 (citing Ex. 1014, Fig. 2-3, 23–25; Ex. 1015 ¶¶ 402–428; Ex. 1022, Figs. 1D, 1E, 70–71, 73, 80, 87).

We already found, in the context of Petitioner’s anticipation contentions, that Klein discloses all of the limitations of independent claims 1 and 13, from which claims 11 and 22 depend, respectively. We further find that both Klein and Tate disclose cart structures for radioactive pharmaceuticals. Ex. 1014, 23–24, Fig. 2-2; Ex. 1022, Figs. 1A–1E, ¶¶ 7,

276). We also find that Tate discloses a cabinet structure that incorporates a shielding structure as well as GUI 15 connected to controller 5. Ex. 1022 ¶¶ 70–71, 73, 80 (describing controller 5 and GUI 15), 87 (describing radioactive shielding on recessed portions of system). We further credit Petitioner’s declarant testimony because the relied-upon portions of Klein support that testimony. Ex. 1015 ¶¶ 402–428 (citing Ex. 1014, Fig. 2-3, 23–25; Ex. 1022, Figs. 1D, 1E, 70–71, 73, 80, 87). Patent Owner does not address these limitations or Petitioner’s related arguments and evidence, or argue that the Klein-Tate combination fails to disclose any of these limitations. See PO Resp. 8–21.

Because Klein and Tate each teach the use of a shielding assembly that includes a cabinet structure, and Tate teaches including the shielding assembly within the cabinet that also carries a computer and controller, Petitioner persuades us by a preponderance of the evidence that the Klein-Tate combination discloses the limitations of claims 11 and 22.

3. Reason to Combine

Petitioner contends that one of ordinary skill in the art would have been motivated to combine Klein and Tate. Pet. 57–59 (citing Ex. 1014, 1, 17, 19, 23, 25; Ex. 1015 ¶ 393–397; Ex. 1022 ¶¶ 2, 9–10, 70, 73, 79, 81, 84, 87, 89–90, 96, 161, 276; Exs. 1023–1024; Exs. 1027–1029; Ex. 1030, 664–710). More specifically, Petitioner argues that (1) “Klein and Tate are both directed to similar subject matter: infusion systems built on portable carts”; (2) “both references disclose application to rubidium-82 elution”; (3) “both references acknowledge the need to minimize radiation exposure, and that incorporation of radioactive shielding is a reliable solution for this problem”; and (4) Klein’s system is a prototype device ripe for obvious design

improvements. *Id.* Petitioner also argues that one of ordinary skill in the art would have had a reasonable expectation of success in making the combination because the combination involves the “simple substitution of one known element for another.” *Id.* at 59–60 (citing Ex. 1013, 23; Ex. 1015 ¶ 399). Patent Owner does not provide arguments as to the motivation to combine issue with respect to Klein and Tate.

Based on the full record, we agree with Petitioner that these references are directed to similar subject matter and share common goals such as minimizing radiation exposure. *See* Ex. 1015 ¶¶ 396–397. Petitioner also persuades us by a preponderance of the evidence that given these similarities and the nature of Klein’s prototype system, that one of ordinary skill in the art would have looked to Tate for further design ideas to incorporate in Klein, including adding shielding within the cabinet structure. *Id.* at ¶ 397–398. We are also persuaded that one of skill in the art would have viewed the substitution of Klein’s shielding assembly with Tate’s as a simple substitution of one known element for another. *Id.* at ¶ 399. We credit Petitioner’s declarant testimony regarding the reason to combine because the record supports it. Ex. 1015 ¶¶ 393–399 (citing Ex. 1014, 1, 16–17, 19, 23, 25–26, 33, 72; Ex. 1022 ¶¶ 2–11, 29, 70, 73, 79, 81, 84, 87, 89–90, 96, 161, 276; Exs. 1023–1024).

4. Conclusion for Obviousness Challenge Based on Klein and Tate

“Once all relevant facts are found, the ultimate legal determination [of obviousness] involves weighing of the fact findings to conclude whether the claimed combination would have been obvious to an ordinary artisan.”

Arctic Cat Inc. v. Bombardier Recreational Prods. Inc., 876 F.3d 1350, 1361 (Fed. Cir. 2017) (quoting *In re Cyclobenzaprine Hydrochloride Extended-*

Release Capsule Patent Litig., 676 F.3d 1063, 1068–69 (Fed. Cir. 2012)).

Above, based on full record before us, we provide our factual findings regarding (1) the level of ordinary skill in the art, (2) the scope and content of the prior art, (3) any differences between the claimed subject matter and the prior art, and (4) objective evidence of nonobviousness.⁸

In particular, we find that (1) Petitioner’s proposed level of ordinary skill in the art is consistent with the prior art of record; (2) the asserted references teach all the limitations of claims 11 and 22; (3) one of ordinary skill in the art would have had a reason to combine Klein with Tate, with a reasonable expectation of success; and (4) there is no objective evidence of nonobviousness in the record. Weighing these underlying factual determinations, a preponderance of the evidence persuades us that claims 11 and 22 of the ’467 patent are unpatentable over Klein and Tate.

F. Challenge Under 35 U.S.C. § 103 Based on Klein and the Bracco Manual

Petitioner challenges claims 8 and 21 as unpatentable over Klein and the Bracco Manual. Pet. 64–67. For these challenges, Petitioner cites to the asserted references and declarant testimony. *Id.* With the exception of Patent Owner’s argument that the Bracco Manual is not prior art to the ’467 patent, Patent Owner does not address Petitioner’s challenge of claims 8 and 21. *See* PO Resp. 19; PO Sur-Reply 8–10.

We summarized the content of Klein above. We begin our analysis by summarizing the Bracco Manual and addressing whether the Bracco

⁸ Petitioner states that it is unaware of any objective evidence of nonobviousness regarding the challenged claims. Pet. 60. Patent Owner does not present any objective evidence of nonobviousness. *See generally* PO Resp.; PO Sur-Reply.

Manual constitutes a prior art printed publication, then address Petitioner's arguments and evidence as to whether the Klein-Bracco Manual combination discloses the limitations of claim 11 and 22, and Petitioner's proffered reasons to combine the references.

1. *The Bracco Manual (Ex. 1021)*

a. *Pertinent Disclosures*

The Bracco Manual is a user's guide for the Rb-82 Infusion System manufactured by Bracco Diagnostics Inc. Ex. 1021, cover. The cover indicates that the Rb-82 Infusion System was manufactured by RbM Services, LLC for Bracco Diagnostics Inc. *Id.*

"The Rb-82 Infusion System is a complete system for the generation and delivery of Rb-82 from a CardioGen[®]-82 generator (Sr-82/Rb-82 generator) to a patient for cardiovascular nuclear medicine procedures," and the Rb-82 is "eluted in sterile normal saline for direct injection into a patient." *Id.* at 1.

The Bracco Manual's system "is a mobile, self-contained cart complete with a shield for a CardioGen[®]-82 generator, a waste bottle shield, a saline syringe pump, sterile tubing and valve components, a positron detector, and all of the support electronics necessary to administer controlled levels of Rb-82 activity to a patient." *Id.* Figure 2.2 of the Bracco Manual is reproduced below.

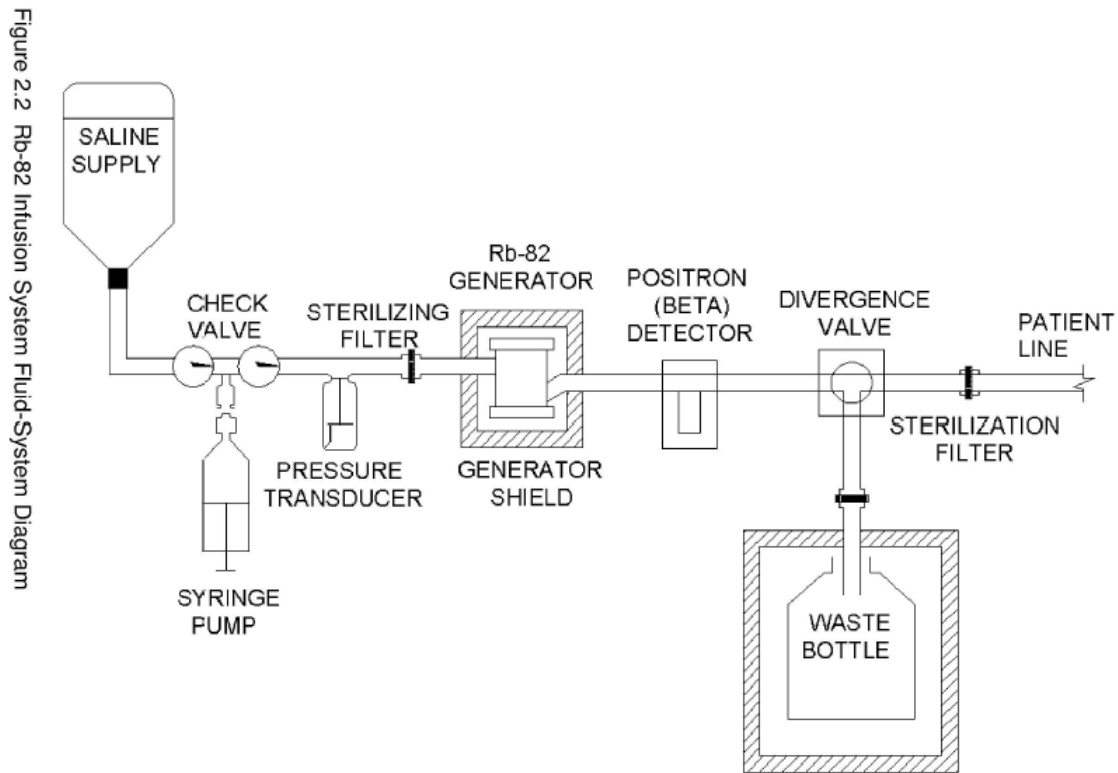


Figure 2.2 is a “Rb-82 Infusion System Fluid-System Diagram.”

Ex. 1021, 3. The Bracco Manual states that “[o]nce an automatic infusion is started, saline is pumped through the generator and the resulting eluate is routed to the waste bottle until its dose rate (mCi/sec) exceeds the pre-selected dose-rate threshold” and “[i]t typically takes 10 to 18 seconds before eluate leaving the generator becomes sufficiently concentrated to reach the required dose-rate threshold of 1.0 mCi/sec.” *Id.* at 4. “Once the dose-rate threshold is exceeded, the Rb-82 eluate is directed to the patient line and both the patient dose and patient volume are measured and displayed.” *Id.*

The Bracco Manual cautions that patient administration should be performed only after completing daily calibration and breakthrough procedures. *Id.* at 31; *see also id.* at 34–35 (providing “Sr-82/85 Breakthrough Worksheet”), 37 (providing “Rb-82 Infusion System

Calibration Log Sheet”). It also states that “[a]t the end of an infusion operation, a complete report of the Rb-82 infusion is printed on the system printer and this same data is echoed out the RS-232C serial data port.” *Id.* at 17.

b. Whether the Bracco Manual Is Prior Art

Patent Owner argues that the Bracco Manual does not qualify as a printed publication because “the manual was only supplied to customers and all such customers were under an obligation of confidentiality during the relevant time period.” PO Resp. 19 (citing *Cordis Corp. v. Boston Scientific Corp.*, 561 F.3d 1319, 1333–1334 (Fed. Cir. 2009)).

Petitioner replies that the Bracco Manual qualifies as a printed publication because Patent Owner “admits that it distributed the printed manual to an interested segment of the public—users of its commercially-available CardioGen system” and “did so for a product that has been commercially available since 1989, roughly two decades before the earliest priority date claimed by the ’467 patent.” Pet. Reply 13 (citing PO Resp. 6, 19; Ex. 1002 ¶¶ 30–33). Petitioner also argues that “the manual (Ex. 1021) contains no confidentiality markings or other language restricting its use.” *Id.* at 13–14; *see also id.* at 14–15 (citing *Nobel Biocare Services AG v. Intradent USA, Inc.*, 903 F.3d 1365, 1377 (Fed. Cir. 2018)). According to Petitioner, Patent Owner does not show *Cordis* applies because there is no showing that confidentiality of the manual was requested and maintained. *Id.* at 14–15. Petitioner further argues that Patent Owner provides no evidence that customers were under an obligation of confidentiality or that the manual was distributed with an expectation that it would be kept confidential and not disseminated, and, thus, “[i]ts contention is mere

attorney argument” that “should be disregarded.” *Id.* at 14 (citing *Icon Health & Fitness, Inc. v. Strava, Inc.*, 849 F.3d 1034, 1043 (Fed. Cir. 2017)).

Patent Owner replies that Petitioner has the burden of showing the Bracco Manual qualifies as prior art by a preponderance of the evidence and that Petitioner has provided no evidence of public accessibility. PO Sur-Reply 8–9. Patent Owner states that “Petitioner did not seek any discovery on this issue from Bracco, did not depose Bracco’s expert, and did not seek to file supplemental information.” *Id.* at 9. Patent Owner argues that “the evidence consists of the Bracco Manual, which lists a 2004 date and says nothing about public accessibility, and Bracco’s explanation that the document was only disseminated to its customers under an obligation of confidentiality.” *Id.* at 9.

Whether a reference qualifies as a “printed publication” is a legal conclusion based on underlying factual findings. *Nobel*, 903 F.3d at 1375 (citing *Jazz Pharm., Inc. v. Amneal Pharm., LLC*, 895 F.3d 1347, 1356 (Fed. Cir. 2018)). The underlying factual findings include whether the reference was publicly accessible. *Id.* (citing *In re NTP, Inc.*, 654 F.3d 1279, 1296 (Fed. Cir. 2011)). The determination of whether a document is a “printed publication” under 35 U.S.C. § 102 “involves a case-by-case inquiry into the facts and circumstances surrounding the reference’s disclosure to members of the public.” *Medtronic, Inc. v. Barry*, 891 F.3d 1368, 1380 (citing *In re Klopfenstein*, 380 F.3d 1345, 1350 (Fed. Cir. 2004)).

A “petitioner need not establish that specific persons actually accessed or received a work to show that the work was publicly accessible.” *Samsung Elecs. Co. v. Infobridge Pte. Ltd.*, 929 F.3d 1363, 1374 (Fed. Cir. 2019). “In fact, a limited distribution can make a work publicly accessible under certain

circumstances.” *Id.* (quoting *GoPro, Inc. v. Contour IP Holding LLC*, 908 F.3d 690, 694 (Fed. Cir. 2018)). “Because there are many ways in which a reference may be disseminated to the interested public, ‘public accessibility’ has been called the touchstone in determining whether a reference constitutes a ‘printed publication’ bar under 35 U.S.C. § 102(b).” *Blue Calypso, LLC v. Groupon, Inc.*, 815 F.3d 1331, 1348 (Fed. Cir. 2016) (quoting *In re Hall*, 781 F.2d, 897, 898–99 (Fed. Cir. 1986)). “A given reference is ‘publicly accessible’ upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it.” *SRI Int’l, Inc. v. Internet Sec. Sys., Inc.*, 511 F.3d 1186, 1194 (Fed. Cir. 2008).

Although not dispositive, the Bracco Manual has a date of “July 20, 2004” and “Rev 07.” Ex. 1021, i; see *Nobel Biocare*, 903 F.3d at 1377 (“Although the ABT Catalog’s date is not dispositive of the date of public accessibility, its date is relevant evidence that supports the Board’s finding of public accessibility at the March 2003 IDS Conference.”); see also PO Sur-Reply 9 (arguing that “the evidence consists of the Bracco Manual, which lists a 2004 date and says nothing about public accessibility, and Bracco’s explanation that the document was only disseminated to its customers under an obligation of confidentiality”). Also, because the Bracco Manual calls itself an “Rb-82 Infusion System User’s Guide” (Ex. 1021, i), we determine that it must have been distributed to purchasers of the Rb-82 Infusion System. See PO Resp. 19 (stating that “the manual was only supplied to customers and all such customers were under an obligation of confidentiality during the relevant time period”). Klein

indicates that either the system described by the Bracco Manual or one like it was known. Ex. 1014, 8 (“Various vendors [Bracco, 2004, formerly Squibb] and research teams have manufactured $^{82}\text{Sr}/^{82}\text{Rb}$ generators that are all similar in design.”).

We further agree with Petitioner that Patent Owner states that “it distributed the printed manual to an interested segment of the public—users of its commercially-available CardioGen system” and “did so for a product that has been commercially available since 1989, roughly two decades before the earliest priority date claimed by the ’467 Patent.” Pet. Reply 13 (citing PO Resp. 6, 19; Ex. 1002 ¶¶ 30–33). Moreover, the Bracco Manual has no indications that it was meant to be confidential or its use restricted, and the record does not indicate that confidentiality was requested or maintained. For the reasons above, Petitioner persuades us by a preponderance of the evidence that the Bracco Manual was publicly accessible in the pertinent time frame.

2. Dependent Claims 8 and 21

Claim 8 depends from claim 7, and claim 21 depends from claim 20. Ex. 1001, 24:20–21, 25:5–6. Both claims require a “given level of activity” of “approximately 1.0 millicurie per second” as indicating eluate may be delivered to the patient. *Id.* Petitioner contends that claims 8 and 21 are unpatentable over Klein and the Bracco Manual. Pet. 64–67. A claim chart includes citations to where the asserted references teach limitations of claims 8 and 21, with citations to supportive declarant testimony. *Id.* at 67. Petitioner states that although Klein teaches all of the limitations of claims 7 and 20, from which claims 8 and 21 depend, Klein fails to “disclose any specific level of activity, such as 1.0 millicurie per second.” *Id.* at 64.

Petitioner contends that the “Bracco Manual discloses diversion of eluate to a waste bottle until activity reaches 1.0 millicurie per second (1.0mCi/sec).” *Id.* (citing Ex. 1021, 4); *see also id.* at 67 (citing Ex. 1015 ¶¶ 438–451; Ex. 1021, 4).

We find that the Bracco Manual describes a “required dose-rate threshold of 1.0mCi/sec,” and that threshold discloses the claimed activity of “approximately 1.0 millicurie per second.” Ex. 1021, 4. We also credit Petitioner’s declarant testimony regarding claims 8 and 21 because the record supports it. Ex. 1015 ¶¶ 438–451 (citing Ex. 1021, 4). Patent Owner does not provide an argument disputing the teachings of Klein and the Bracco Manual with respect to claims 8 and 21. *See* PO Resp. 19.

Based on the full record, because the Bracco Manual teaches the claimed activity and Klein teaches the other limitations, Petitioner persuades us by a preponderance of the evidence that the combination of Klein and the Bracco Manual teaches the limitations of claims 8 and 21.

3. Reason to Combine

Petitioner contends with declarant testimony support that one of ordinary skill in the art would have been motivated to combine the teachings of these references because (1) the Bracco Manual “describes well known operating procedures for rubidium-82 elution systems” that would provide a natural reference for specific activity levels in such systems; (2) Klein suggests delivering eluate until a specific activity level is reached, and the Bracco Manual “provides more detail of what that activity level should be”; and (3) the references “are both directed to similar subject matter: infusion systems built on a portable cart for use in patient procedures.” Pet. 65–66 (citing Ex. 1014, 1, 7–13, 17, 19, 23, 44–45; Ex. 1015 ¶¶ 432–435; Ex.

1021, 1, 33). Petitioner additionally contends that one of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings of Klein and the Bracco Manual because the combination “simply requires selection of a parameter—the activity level of the eluate.” *Id.* at 66–67 (citing Ex. 1015 ¶ 436). Patent Owner does not provide arguments as to the motivation to combine issue with respect to Klein and the Bracco Manual.

Based on the full record, we agree with Petitioner that these references are directed to similar matter and address common issues such as the specific activity level at which to begin elution delivery to the patient, and the Bracco Manual provides more detail on the subject that one of ordinary skill in the art would find helpful to implement in Klein’s system. *See* Ex. 1015 ¶¶ 433–435. We are also persuaded that one of skill in the art would have viewed the use of the Bracco Manual’s specific activity level in Klein’s system as likely to lead to success given its use in the similar system the Bracco Manual discloses. *Id.* at ¶ 436. We credit Petitioner’s declarant testimony regarding the reason to combine because the record supports it. Ex. 1015 ¶¶ 433–436 (citing Ex. 1014, 1, 7–13, 17, 19, 23, 44–45; Ex. 1021, 1, 33; Ex. 1022 ¶¶ 2, 70, 81, 89–90, 96, 161).

4. Conclusion for Obviousness Challenge Based on Klein and the Bracco Manual

“Once all relevant facts are found, the ultimate legal determination [of obviousness] involves weighing of the fact findings to conclude whether the claimed combination would have been obvious to an ordinary artisan.” *Arctic Cat*, 876 F.3d at 1361. Above, based on full record before us, we provide our factual findings regarding (1) the level of ordinary skill in the art, (2) the scope and content of the prior art, (3) any differences between the

claimed subject matter and the prior art, and (4) objective evidence of nonobviousness.⁹

In particular, we find that (1) Petitioner's proposed level of ordinary skill in the art is consistent with the prior art of record; (2) the asserted references teach all the limitations of claims 8 and 21; (3) one of ordinary skill in the art would have had a reason to combine Klein with the Bracco Manual, with a reasonable expectation of success; and (4) there is no objective evidence of nonobviousness in the record. Weighing these underlying factual determinations, a preponderance of the evidence persuades us that claims 8 and 21 of the '467 patent are unpatentable over Klein and the Bracco Manual.

⁹ Petitioner states that it is unaware of any objective evidence of nonobviousness regarding the challenged claims. Pet. 67. Patent Owner does not present any objective evidence of nonobviousness. *See generally* PO Resp.; PO Sur-Reply.

IV. CONCLUSION¹⁰

In summary:

Claims	35 U.S.C. §	Reference(s)/Basis	Claims Shown Unpatentable	Claims Not shown Unpatentable
1–4, 6, 7, 9, 10, 12– 16, 18–20	102(b)	Klein	1–4, 6, 7, 9, 10, 12–16, 18–20	
11, 22	103(a)	Klein, Tate	11, 22	
8, 21	103(a)	Klein, Bracco Manual	8, 21	
Overall Outcome			1–4, 6–16, 18–22	

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1–4, 6–16, and 18–22 of U.S. Patent No. 9,299,467 B2 have been shown, by a preponderance of the evidence, to be unpatentable; and

FURTHER ORDERED that, because this is a Final Written Decision, the parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

¹⁰ Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner’s attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*. See 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. See 37 C.F.R. § 42.8(a)(3), (b)(2).

IPR2018-01449
Patent 9,299,467 B2

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