

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MIM SOFTWARE INC.,
Petitioner,

v.

PROGENICS PHARMACEUTICALS, INC.,
Patent Owner.

IPR2025-00725
U.S. Patent No. 11,424,035

PATENT OWNER'S PRELIMINARY RESPONSE

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EX2001	Defendant's Memorandum of Law in Support of its Motion to Stay Pending <i>Inter Partes</i> Review, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 89, Apr. 8, 2025.
EX2002	PACER Docket, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS (as of June 11, 2025).
EX2003	Defendant's Motion to Dismiss the Second Amended Complaint, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 43, June 17, 2024.
EX2004	Motion to Dismiss Hearing Transcript (excerpted pp. 1, 4-6), <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Oct. 8, 2024.
EX2005	Order Granting in Part and Denying in Part Defendant's Motion to Dismiss the Second Amended Complaint, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 72, Jan. 14, 2025.
EX2006	Motion to Stay Hearing Transcript (excerpted pp. 1, 5-6), <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, May 12, 2025.
EX2007	Order Granting in Part and Denying in Part Defendant's Motion to Stay Pending <i>Inter Partes</i> Review, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 102, May 13, 2025.
EX2008	MIM's Invalidity and Noninfringement Contentions, Civil Action No. 1:24-cv-10437-PBS.
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EX2011	<i>Cancer Control Month, 2025 – The White House</i> (Apr. 3, 2025).
EX2012	<i>NIH Strategic Plan for Data Science FY 2025-2030</i> , Nat'l Institutes of Health.
EX2013	Rowe, S.P. et al., <i>PET Imaging of Prostate-Specific Membrane Antigen in Prostate Cancer: Current State of the Art and Future Challenges</i> , Prostate Cancer & Prostatic Diseases (2016).
EX2014	Declaration of Dr. Milan Sonka.
EX2015	Curriculum Vitae of Dr. Milan Sonka.
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EX2018	<i>PET Scans</i> , CancerQuest, Emory Winship Cancer Institute (2025).
EX2019	Rowe, S.P., et al., <i>PSMA-Based [¹⁸F]DCFPyL PET/CT Is Superior to Conventional Imaging for Lesion Detection in Patients with Metastatic Prostate Cancer</i> , Molecular Imaging and Biology 18(3):411-419 (2016).
EX2020	<i>FDA Approves First PSMA-Targeted PET Imaging Drug for Prostate Cancer</i> , Oncology Practice Management (2020).
EX2021	<i>FDA Approves Second PSMA-Targeted PET Imaging Drug for Men with Prostate Cancer</i> , Food and Drug Administration (2021).
EX2022	<i>Atlas-Based vs. AI Auto-Contouring in Clinical Practice</i> , MIM Software Inc. (2023).
EX2023	Brown, <i>Machine Learning, Explained</i> , MIT Sloan (Apr. 21, 2021).
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EX2026	Deng, et al., <i>ImageNet: A large-scale hierarchical image database</i> , IEEE Conference on Computer Vision and Pattern Recognition (2009).
EX2027	Bushberg, J.T., et al., <i>The Essential Physics of Medical Imaging</i> (2012), Ch. 1, Sec. 1.1, pp. 3-15.
EX2028	Bushberg, J.T., et al., <i>The Essential Physics of Medical Imaging</i> (2012), Ch. 3, Sec. 3.1, pp. 33-38.
EX2029	Kelleher, <i>Deep Learning</i> (2019), Ch. 1, “What Is Machine Learning?,” pp. 9-17.
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EX2032	Kelleher, <i>Deep Learning</i> (2019), Ch. 4, “The Era of Deep Learning,” pp. 143-145.
EX2033	Kelleher, <i>Deep Learning</i> (2019), Ch. 4, “Layer-Wise Pretraining Using Autoencoders,” pp. 145-148.
EX2034	Kelleher, <i>Deep Learning</i> (2019), Ch. 4, “Weight Initialization and ReLU Activation Functions,” pp. 148-153.
EX2035	Kelleher, <i>Deep Learning</i> (2019), Ch. 4, “The Virtuous Cycle: Better Algorithms, Faster Hardware, Bigger Data,” pp. 153-156.

I. INTRODUCTION

U.S. Patent No. 11,424,035 (the “’035 Patent”) discloses a novel and inventive solution to serious challenges that doctors faced when analyzing medical images to diagnose, monitor and treat cancer. More specifically, the ’035 Patent claims an inventive process for taking anatomical and functional images, automatically segmenting organs, identifying regions of cancer within relevant organs, and then creating a risk map that demarcates cancer risk.

Among other things, the key advances of the ’035 Patent include systems and methods that incorporate specific machine learning-based techniques that are tailored to, and provide innovative solutions for, the analysis of specific types of medical images, and a network-based system approach that is particularly valuable in the context of cancer diagnosis and treatment.

For example, the ’035 Patent recognized that machine learning (ML) algorithms could be used to geographically identify 3D boundaries of particular tissue regions in a more accurate and robust manner than had been possible previously. Moreover, the ’035 Patent applied this approach specifically to identifying organs from a CT scan using ML-based segmentation, then creating a composite of the segmented CT scan overlaid with a nuclear medicine image, such as a 3D PET or SPECT image. This is especially inventive and valuable because, as described in the ’035 Patent, nuclear medicine images are often best suited to

identify cancer. *See* EX1001, 15:43-64. However, they are limited in their ability to capture features of anatomy and structure of organs and/or tissues, for example, at sufficiently high resolution. EX2014, ¶¶27-30, 57; *see also* EX1001, 27:16-40. In this way, one can more accurately identify 3D boundaries of organs, thereby adding valuable anatomical context to the nuclear medicine image, where it is often lacking.

The '035 Patent also recognized that it would be especially valuable for cloud-based systems of cancer diagnosis/treatment if one could take advantage of remote networking by uploading medical images to, and accessing them from, databases via network-based systems.

Finally, the '035 Patent leverages particular radiopharmaceuticals – PSMA binding agents – that, around the time of filing, were in the early stages of being studied for their potential for prostate cancer diagnosis. EX2014, ¶89; *see also id.*, ¶34. The '035 Patent thus combines insight into the promise of those imaging agents, together with the above-described image analysis techniques and network-based delivery platform, to provide a comprehensive solution tailored for assisting physicians and patients with prostate cancer diagnosis, monitoring, and treatment.

None of the references that Petitioner relies on teaches or suggests this unique combination of features, which are recited in the claims of the '035 Patent. Instead, for its main grounds against the independent claims, the Petition relies on a

combination of three references that are directed to fundamentally distinct and incompatible techniques. Petitioner fails to adequately explain why a POSA would have been motivated to combine such fundamentally different asserted references with any reasonable expectation of success.

Therefore, Patent Owner requests that the Board deny institution of the Petition.

II. TECHNOLOGY BACKGROUND

One major challenge in treating and managing cancer (and other serious diseases) has long been the difficulty of accurately and consistently interpreting the diagnostic images produced by medical imaging tools. *See* EX2014, ¶¶35, 55. Both anatomical scans (like X-rays or CT) and functional scans (like PET or single-photon emission computed tomography (SPECT)) are valuable tools. EX2014, ¶¶26-28. But before the inventions claimed in the '035 Patent, physicians faced major obstacles in using those scans to form a complete and trustworthy picture of a patient's disease.

One difficulty was that each type of scan could only capture part of the relevant picture for any given patient. Simply put, anatomical scans capture images of the anatomy or structure of organs and tissues within the body (but not the function); functional scans capture the activity and function of those organs or tissues (but not the anatomy/structure). *See* EX2014, ¶¶27-28. As applied to cancer,

an anatomical scan thus cannot reliably detect the activity of a tumor, whereas a functional scan can struggle to differentiate between the organs and tissue surrounding a tumor. *See* EX2014, ¶¶27-28. Physicians were left to parse two different types of scans to try to piece together the full picture, and this often led to inaccurate or inconsistent diagnoses or treatments.

While radiologists and physicians have various medical imaging modalities and techniques at their disposal, the selection of which types of images to obtain, and how to interpret these images is not straightforward. EX2014, ¶35. To the contrary, the task of determining, for example, whether a particular patient has cancer, how severe it is, and what course of action to take is laborious, error prone, and highly subjective, often varying from physician to physician. EX2014, ¶35. Without effective automated integration, mapping, and assessment of scan results, a physician might miss a critical diagnostic insight.

III. CITED REFERENCES

A. Maier

Maier is directed to a “computer implemented method for assessing and communicating a patient’s health status and risk.” EX1005, [0007]; EX2014, ¶50. Maier is concerned primarily with smoking-related diseases like “myocardial infarction, Chronic Obstructive Pulmonary Disease (COPD), emphysema, lung cancer, decreased lung function, COPD exacerbations, coronary artery disease, and

stroke.” EX1005, [0007]; EX2014, ¶50. Maier’s approach for assessing patient risk involves extracting values of image features such as numbers or percentages of voxels with certain intensities, mean image intensities, complex texture features, etc. and using them as, what he calls, “imaging biomarkers,” presumably by way of analogy to conventional, e.g., genetic or molecular biomarkers. EX1005, [0007]-[0008]; EX2014, ¶50. Maier correlates values of imaging biomarkers determined for a given patient with values from historical patient populations having known clinical outcomes – similar to how, for example, the BRCA1 and BRCA2 genes are genetic biomarkers for breast cancer risk and cholesterol levels are biomarkers for risk of heart disease. EX1005, [0007]-[0008]; EX2014, ¶50.

B. Huang

Huang discloses a method for analyzing digitized images for body landmark modeling and detection. EX1006, [0002], [0014]. Huang’s method is directed to applications related to CAD tools for fluorine-18 deoxyglucose (FDG) uptake imaging. EX1006, [0003], [0006], [0051], [0098], [0108]; EX2014, ¶51.

C. Armor

Armor discloses Tc-99m labeled PSMA targeting agents (a gamma-emitting transition metal complex conjugated to a targeting moiety), suitable for SPECT imaging. EX1007, [0008]; EX2014, ¶52. Armor also describes a method of evaluating a human subject suspected of harboring a prostate tumor that uses his

SPECT imaging compounds, but otherwise appears to involve conventional SPECT/CT imaging techniques and analysis. EX1007, [0096] (requiring a user to manually place “[c]ircular regions of interest with a diameter of approximately 20 pixels” on regions adjacent to the prostate gland and recording counts in that region as background); EX2014, ¶52.

D. Neumaier, Giesel, and Weineisen

Neumaier (EX1008), Giesel (EX1010), and Weineisen (EX1011) each describe specific methods for synthesizing particular radiopharmaceutical compounds or analyses of their characteristics, via otherwise conventional imaging techniques. EX1008, Abstract, 1:1-13; EX1010, 1929; EX1011, 1169, 1171; EX2014, ¶53.

IV. THE '035 PATENT

A. The Invention

As of the priority date (October 27, 2016), there remained a critical need for innovative solutions to increase the accuracy, reliability, and consistency of medical imaging analysis, especially for (but not limited to) cancer diagnosis and treatment. EX2014, ¶55. The '035 Patent addresses this need by providing image analysis technologies that take advantage of machine learning techniques and implement them in specific ways to analyze specific types of medical images. EX2014, ¶55; *see also id.*, ¶54. Further, the technology described in and claimed by the '035 Patent delivers these capabilities in the format of a network-based platform, which the '035

Patent recognized would be valuable for cancer diagnosis and treatment. EX2014, ¶55.

In particular, the '035 Patent describes inventive processes for accessing anatomical and functional images, automatically segmenting organs, identifying regions of cancer within relevant organs, and then creating a risk map that demarcates cancer risk. EX2014, ¶56.

The '035 Patent thus reflects multiple key innovations, and leverages insight into how they could be combined in a synergistic fashion, to provide a valuable tool for tracking and aiding physicians over the course of a patient's prostate cancer progression and treatment. *See* EX2014, ¶57.

One of those innovations was to leverage machine learning ("ML") techniques, including, but not limited to, convolutional neural networks ("CNNs") to perform organ segmentation in 3D images (e.g., 3D CT scans). EX2014, ¶57; *see also id.*, ¶¶44-49. The '035 Patent recognized that ML could be used to geographically identify 3D boundaries of particular tissue regions in a more accurate and robust manner with desirable scan-to-scan reproducibility than had been possible previously. *Id.*

More particularly, the '035 Patent implemented ML-based segmentation of CT scans to accurately and robustly identify tissue regions (e.g., organs). EX2014, ¶57. It also recognized the benefit of forming a composite image comprising the

segmented CT scan overlaid with a nuclear medicine image (e.g., PET or SPECT image). *See id.* The overlay of the ML-segmented CT scan and the nuclear medicine image allows the accurately identified tissue regions to be used together with the functional information of the nuclear medicine image to create a cancer risk map. *Id.*

This is especially significant because, as described in the '035 Patent, cancer is often best detected via nuclear medicine imaging approaches, like 3D PET or 3D SPECT. *See id.* Nuclear medicine techniques, however, do not capture features of anatomy and structure of organs and/or tissues at sufficiently high resolution. *Id.* They thus cannot always reliably distinguish between different organs or tissue regions. *Id.*; *see also id.*, ¶¶28-30. The '035 Patent's approach allows 3D boundaries of organs to be more accurately identified, and valuable anatomical context to be added to the nuclear medicine image, where it is often impossible to obtain, inaccurate, or subjective. *Id.*, ¶57. Leveraging the highly sensitive functional image information provided by nuclear medicine images together with accurate 3D boundaries of tissue regions obtained via ML-based segmentation (e.g., of CT images) allows, for example, improved risk maps that accurately identify cancer risk to be computed. *Id.*

Another key innovation of the '035 Patent was combining the insight about ML techniques with the insight that taking advantage of remote networking by

uploading medical images to, and accessing them from, databases via network-based systems would be especially valuable in the context of cancer diagnosis in treatment. *Id.*, ¶58.

Finally, the '035 Patent leverages particular radiopharmaceuticals – PSMA binding agents – that, around the time of filing, were in early stages of being studied for its potential for prostate cancer diagnosis. *Id.*, ¶59; *see also id.*, ¶34. The '035 Patent thus combines insight into the promise of those imaging agents together with the above-described image analysis techniques and network-based platform delivery platform to provide a comprehensive solution tailored for assisting physicians and patients from prostate cancer diagnosis, to monitoring, and through treatment. *Id.*, ¶59.

As such, the claimed methods provide numerous advantages over prior art methods. *Id.*, ¶60.

B. Prosecution History

The Application for the '035 Patent was filed on July 14, 2020, claiming priority to U.S. Provisional Application 62/413,936 filed on October 27, 2016. EX1004, 114. The '035 Patent issued on August 23, 2022. EX1004, 287; EX2014, ¶61.

During prosecution, the Examiner identified six references on his “Notice of References Cited.” EX1004, 236; EX2014, ¶63. Two of these references were

exactly the Huang and Maier references that the Petition now relies, primarily, on in their challenges against the claims in the '035 Patent. EX1004, 236; EX2014, ¶¶62-63. The '035 Patent also cited the Petition's third main reference, Armor, in an IDS submitted to the Office on May 27, 2021. *See* EX1004, 179; EX2014, ¶63. On April 22, 2022, the Examiner also signed the IDS, noting at the bottom that "ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.H.A./." The Examiner did not line through the Armor reference. *See* EX1004, 267; EX2014, ¶63. On April 19, 2022, as reflected in the Examiner's interview summary, the Examiner conducted "a telephone interview, which was initiated by the examiner with applicant's representative," and "**after discussing all prior art of record**, examiner suggests ways to clarify the independent claim or amend the claim that may overcome the prior art of record" EX1004, 235 (emphasis added); EX2014, ¶64. The Examiner thus allowed the claims after considering the Maier, Huang, and Armor references and requesting amendments to the independent claims to overcome the art. *See* EX2014, ¶¶64-65. In the Notice of Allowance, the Examiner highlighted the following key features that appear in independent claim 1 of the '035 Patent:

automatically analyze the one or more medical images using a machine learning algorithm; wherein the one or more medical images comprise a composite image of the particular patient, the composite image comprising a CT scan "overlaid with a nuclear medicine image" obtained at a substantially same time as the CT scan and following administration to the patient of an imaging agent comprising a Prostate

Specific Membrane Antigen (PSMA) binding agent comprising a radionuclide, wherein the instructions cause the processor to automatically analyze the composite image by: using the composite image to geographically identify a 3D boundary for each of one or more regions of imaged tissue within the nuclear medicine image; and computing, using the nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s), a risk map comprising a “graphical denotation marking a region” of risk of cancer or risk of recurrence of cancer”.

EX1004, 232-33; EX2014, ¶65.

Thus, the three references that form the basis of the Petition’s challenges against the independent claims in the ’035 Patent are not new – they were already considered during prosecution of the ’035 Patent. EX2014, ¶66.

V. PERSON OF ORDINARY SKILL

Petitioner argues that a POSA “would include a person with a medical (MD) degree and/or an advanced degree in Computer Engineering, Computer Science, Physics, or other field related to computer imaging, and at least 3 years of field experience with medical imaging devices, such as PET/CT or SPECT/CT systems.” Pet., 8-9; EX2014, ¶15.

For purposes of this preliminary response, Patent Owner does not dispute Petitioner’s definition of a POSA. EX2014, ¶¶13-16.

VI. CLAIM CONSTRUCTION

Under 37 C.F.R. § 42.104(b), the Petitioner bears the burden to set forth “how the challenged claim is to be construed” and “how the construed claim is unpatentable.” Therefore, when a petition relies on an incorrect claim construction

(either expressly or impliedly), and fails to offer any evidence of unpatentability under the proper claim construction, institution should be denied. *See, e.g., Amazon Web Servs., Inc. v. Saint Regis Mohawk Tribe*, No. IPR2019-00103, Paper 22, 14–15, 17, 19–20 (P.T.A.B. May 10, 2019) (denying institution); *Jiawei Tech. Ltd. v. Richmond*, No. IPR2014-00937, Paper 22, 7-8 (P.T.A.B. Dec. 16, 2014) (denying institution where petition did not provide express construction for term and did not adequately explain how term read on cited prior art). Here, the Petition relies on an incorrect construction of important claim terms, and fails to offer evidence of unpatentability for certain grounds under the proper claim construction. Institution should thus be denied. Patent Owner addresses each relevant claim term below.

A. The Petition relies on an incorrect implied construction of “network-based . . . system.”

The term “network-based . . . system” appears in claim 1 of the ’035 Patent. Specifically, in its preamble, claim 1 recites, “A **network-based** decision support **system** comprising . . .” EX1001, 36:18 (emphasis added).

The correct construction of the term “a network-based system” is “a system involving interaction across multiple interconnected and physically dispersed computing devices.” This construction comports with both the claim language and the specification. EX2014, ¶69.

First, the claim language expressly uses the term “a network-based . . . system” (as opposed to simply “a system”), and, accordingly, a POSA would afford

the words “network-based” a meaning more than specific than simply “a system” of any kind. EX2014, ¶¶70-71. Second, the specification affirms that “a network-based . . . system” means a system involving interaction across multiple interconnected and physically dispersed computing devices. *See* EX2014, ¶72. The specification repeatedly describes the ’035 Patent’s claimed technology as a part of a distributed platform, rather than a standalone machine like a simple computer workstation connected to an imaging device. *See id.*, ¶¶72-79. Numerous figures in the ’035 Patent convey interactions between distinct computing devices, such as serve and client devices and members of a cloud-based service, and they are repeatedly described as providing platform-based functionality that allows interaction across multiple interconnected and physically dispersed computing devices. EX1001, FIG. 1 (showing mobile app providing access to three cloud-based services); *id.*, FIG. 2 (showing a schematic showing the relationship between a platform and a computing device); *id.*, FIG. 7 (a block diagram of an exemplary cloud computing environment); *id.*, FIG. 9 (a block diagram of an example architecture for implementing the cloud based platform); EX2014, ¶¶74-77.

Furthermore, the specification of the ’035 Patent repeatedly emphasizes the ability of the network-based platform to provide access to multiple users and to obtain, store, and analyze medical images that are obtained over the course of multiple visits to one or more doctors and/or clinical specialists. *See, e.g.*, EX1001,

30:53-31:7; EX2014, ¶78. Altogether, then, a POSA would understand these various and repeated disclosures to require that “a network-based system” involves multiple physically distinct machines whose interaction occurs across a network. EX2014, ¶79.

In light of both the claim language and the specification, a POSA would understand that “a network-based system” thus refers to a system involving interaction across multiple interconnected and physically dispersed computing devices. *Id.*

B. The Petition relies on an incorrect implied construction of “database.”

The term “database” appears in independent claims 1, 18, 36, and 41 of the ’035 Patent. Steps (i) and (ii) of claims 1 and 18 recite “receiv[ing] and stor[ing], a plurality of medical images in a **database**,” and “access[ing] one or more of the medical images associated with a particular patient from the **database**...,” respectively. EX1001, 36:23-29 (claim 1) (emphasis added); 37:38-44 (claim 18) (similar); EX2014, ¶80. Claims 36 and 41 also recite, *inter alia*, “repeatedly receiving and storing in a **database**, over time, by a processor of a computing device, a plurality of medical images for each of the one or more patient(s) to obtain, for each of the one or more patient(s), a series of medical images taken over time[.]” EX1001, 38:38-39 (claim 36); 40:54-57 (claim 41) (similar) (emphasis added); EX2014, ¶80.

The correct construction of the term “database” is “a large structured set of data that contains multiple records that contain multiple fields.” EX2014, ¶81. This construction comports with both the claim language and the specification. EX2014, ¶81. Moreover, as discussed below, a POSA reading the claims and specification of the ’035 Patent would understand that the term “database” is not synonymous with the term “memory.”

First, the claim language makes clear that a “database” is a persistent, structured repository that is distinct from a processor or memory. EX2014, ¶82. For example, step (ii) of claim 1 teaches “access[ing] one or more medical images associated with a particular patient from the database...” *Id.* A “database” is thus a data set from which the recorded “medical images” can be “access[ed].” *See id.* Second, the specification repeatedly affirms that “database” means a large structured set of data that contains multiple records that contain multiple fields. EX2014, ¶83. For example, when describing the cloud diagram in Figure 7 above, the specification identifies “application servers and/or databases with storage and retrieval capabilities” as discrete network resources, separate from compute nodes. EX1001, 31:43-44; EX2014, ¶83. That language mirrors Plaintiffs’ proposed definition of a database: a store built for structured retrieval.

The specification also describes how the systems and methods of the ’035 Patent “allow[s] multiple users to store, access, analyze, and/or provide feedback

regarding a given set of image data for the patient.” EX1001, 3:1-14; EX2014, ¶¶83-84. Moreover, the specification describes how the claimed invention causes the processor to “repeatedly receive and store in a database over time, a plurality of medical images for each of the one or more patient(s) to obtain, a series of medical images taken over time (e.g., over the course of multiple visits to one or more doctors thereby tracking determined values of the one or more risk indices over a course of prostate cancer progression and treatment for the patient[.]” EX1001, 11:43-64; EX2014, ¶85. This language further affirms that “database” means a structured, multi-record repository that carries multiple records (patients, series, images, etc.) and multiple fields (timestamps, modality, dose, metadata, etc.). *See* EX2014, ¶¶84-85.

In light of both the claim language and the specification, a POSA would understand that a “database” thus refers to a large structured set of data that contains multiple records that contain multiple fields. EX2014, ¶87.

A POSA would also understand, reading the claims in the context of the specification, that “database” is different than “memory.” The claims and specification of the ’035 Patent use the term “database” differently than “memory.” For example, claim 1 begins: “A network-based decision support system comprising: a **processor**; and a **memory** having instructions stored thereon, wherein the instructions, when executed by the processor, cause the processor to: (i) receive

and store a plurality of medical images in a **database...**,” and “access one or more of the medical images associated with a particular patient from the database[.]” EX1001, 36:18-29 (emphasis added); EX2014, ¶82. Other claims make the same distinctions. *See, e.g.*, EX1001, 40:54-57 (claim 41). Reading “database” to mean a simple memory would thus collapse the two expressly different claim terms. *Supra*, 15.

The specification differentiates between the two terms as well. The specification describes “memory” as a hardware element within the computing device, whereas “database” means a structured store of data. *See, e.g.*, EX1001, 32:52-57 (“The memory 804 stores information within the computing device 800. In some implementations, the memory 804 is a volatile memory unit or units. In some implementations, the memory 804 is a non-volatile memory unit or units. The memory 804 may also be another form of computer-readable medium, such as a magnetic or optical disk.”); *id.*, 34:29-37 (“The memory may include, for example, flash memory and/or NVRAM memory The instructions can also be stored by one or more storage devices, such as one or more computer- or machine-readable mediums (for example, the memory 864 . . .”).

VII. THE PETITION DOES NOT ESTABLISH A “REASONABLE LIKELIHOOD” OF UNPATENTABILITY.

Under 35 U.S.C. § 314(a), the Board may not institute inter partes review unless the Petition demonstrates “that there is a reasonable likelihood that the

petition would prevail with respect to at least 1 of the claims challenged in the petition.” This is a threshold requirement, and the burden rests entirely with the Petitioner. *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (“the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable”). Here, the Petition fails to establish a “reasonable likelihood” of unpatentability as to any challenged claim. Institution should thus be denied. Patent Owner addresses each ground below.

A. Ground A: Maier in view of Huang and Armor does not render obvious claims 1-7, 9-24, and 26-35.

The Petition fails to establish a reasonable likelihood that Maier in view of Huang and Armor renders claims 1-7, 9-24, and 26-35 obvious. EX2014, ¶88. Since claims 1 and 18 are the only independent claims, Patent Owner addresses each in turn.

Independent claim 1 is directed to using a “machine learning algorithm” to analyze medical images and generate a risk map that identifies regions of risk of cancer. EX2014, ¶89. As briefly previewed above, the claimed invention includes several key advances for helping physicians track a patient’s prostate cancer progression and treatment. *Id.* For example, the ’035 Patent recognized that machine learning (ML) could be used to geographically identify 3D boundaries of particular tissue regions in a more accurate and robust manner than was previously possible. *Id.* Further, the claimed invention presented a new way of leveraging ML

techniques in the context of a particular type of image – a composite image comprising a CT scan overlaid with a nuclear medicine image obtained via use of a PSMA binding agent. *Id.* At the time the '035 Patent was effectively filed, imaging with PSMA binding agents was just beginning to show promise for sensitive diagnosis of prostate cancer. *Id.*

In particular, the '035 Patent teaches how to analyze a composite image that comprises a CT scan overlaid with a nuclear medicine image acquired using a PSMA binding agent. EX2014, ¶90. The claims describe analyzing these composite images by first using the composite image to identify 3D boundaries of imaged tissue within the nuclear medicine image, and then using the nuclear medicine image with the identified 3D boundaries to compute the risk map. *Id.* This approach is described in detail in the specification of the '035 Patent, for example in Section A.iv (“Positron Emission Tomography (PET) Scans”). *Id.* It leverages the complementary anatomical and functional information provided by the CT scan and nuclear medicine image, respectively, and combines this information by virtue of the overlay between the two images in a composite image, such as a PET/CT or SPECT/CT. *Id.*

The claims of the '035 Patent combine this insight about ML techniques and new imaging approaches with the insight that taking advantage of remote networking by uploading medical images to, and accessing them from, databases via

network-based systems would be especially valuable in the context of, e.g., cloud-based systems for cancer diagnosis and treatment. EX2014, ¶91.

As explained in further detail below, the cited references fail to disclose this unique combination of features. Notably, the Petition acknowledges that its primary reference, Maier, does not disclose key features of Patent Owner's claimed subject matter that are recited in the claims. EX2014, ¶92. Maier does not disclose the particular type of medical images that is recited in claim 1. Maier also does not disclose any radiopharmaceutical, let alone the particular radiopharmaceutical that is used and recited in claim 1. And Maier does not disclose the particular way of analyzing those images that is recited in claim 1. *See id.*

The Petition thus includes two additional references – Huang and Armor – to attempt to cure these key deficiencies in Maier. *See id.* As explained in further detail below, they do not fill Maier's glaring gaps. *See id.* Maier, Huang, and Armor all relate to fundamentally distinct and incompatible approaches for obtaining and analyzing images and have different goals. *See id.* The Petition attempts to skirt this issue by providing element-wise obviousness arguments that gloss over significant incompatibilities between the cited references, and ultimately fail to show that a POSA would be motivated to, or even could, combine them to arrive at the claimed subject matter of the '035 Patent. *See id.*

1. **Maier and Huang do not render obvious the element “wherein the one or more medical images comprise a . . . CT scan overlaid with a nuclear medicine image” as recited in claims 1 and 18.**

Limitation (f)¹ of claim 1 is directed to “generat[ing] a radiologist report for the particular patient according to the one or more medical images for the patient, **wherein the one or more medical images comprise a . . . CT scan overlaid with a nuclear medicine image[.]**” Pet., 26 (claim 1); EX2014, ¶93; claim 18 (similar). The Petition acknowledges that Maier fails to disclose this, but alleges that Huang discloses this element, and that the combination of Maier and Huang thus render this claim element obvious. Pet., 26; EX2014, ¶93.

The Petition fails to demonstrate a reasonable likelihood of unpatentability because it fails to show that a POSA would have been motivated to combine Maier and Huang with a reasonable expectation of success. This is true for at least three reasons.

First, the Petition fails to carry its burden to show motivation to combine because the Petition improperly focuses on individual limitation (f), rather than the claim as a whole. *See KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (“[A] patent composed of several elements is **not proved obvious** merely by

¹ For the sake of convenience, Patent Owner references claim limitations using the Petition's labeling scheme.

demonstrating that each of its elements was, **independently**, known in the prior art.”) (emphasis added); *Env'tl. Designs, Inc. v. Union Oil Co.*, 713 F.2d 693, 698 (Fed. Cir. 1983) (“Virtually all inventions are combinations and virtually all are combinations of old elements. A court must consider what the prior art **as a whole** would have suggested to one skilled in the art[.]”) (emphasis added). Here, however, the Petition argues only that a POSA would have had a motivation to combine Maier and Huang to perform *limitation (f)*, rather than claim 1 as a whole. Pet., 26 (“Maier in view of Huang renders obvious this limitation.”). The Petition makes a similar mistake for several other limitations. Pet., 30 (claim 1(g)); 33 (claim 1(h)); 37 (claim 1(i)). Apart from the conclusory statement at the end of Section B.1 of the Petition (“Therefore, Maier in view of Huang and Armor renders obvious claim 1”), the Petition never presents a sustained and detailed argument for why Maier, Huang, and Armor render any of the entirety of the challenged claims obvious, as is required under 35 U.S.C. § 103. Pet., 42. Instead, the Petition’s motivation to combine argument fails because it improperly proceeds on a limitation-by-limitation basis without sufficiently explaining why a POSA would have been motivated to combine the asserted references to achieve the claim as a whole with a reasonable expectation of success.

Second, the Petition’s limitation-by-limitation approach is especially confusing and unconvincing because, for each individual limitation, the Petition

presents multiple distinct and individualized (e.g., with respect to the particular limitation) arguments about whether a POSA would have a motivation to combine the cited references. For example, for limitation (f), the Petition argues two different options for motivations to combine: (i) “Teaching, suggestion, motivation,” apparently for the specific reason of “Improved physician decision-making” or (ii) “Combination according to known methods to yield predictable results.” Pet. 27-29. Next, for limitation (g), the Petition presents three potential motivations to combine, individualized for this particular limitation: (i) “Teaching, suggestion, motivation,” apparently for the specific reason to “Improve cancer diagnosis and monitoring,” or (ii) “Compatibility with Maier and Huang’s multi-modal imaging,” or (iii) “Simple substitution of one known element for another to obtain predictable results.” Pet. 31-33. For limitation (h), the Petition offers up another mix of individualized motivations to combine. The Petition argues (i) “Teaching, suggestion, motivation,” now on the basis of (a) “Improved, organ-specific identification,” or (b) “Compatibility with machine-learning algorithms” or (ii) “Combining prior art elements according to known methods to yield predictable results,” or (iii) “Known technique to improve similar devices in the same way.” Pet. 35-37. Finally, at limitation (i), the Petition’s motivation to combine cross-references its arguments made in regard to limitations (g) and (h) (though apparently not those in regard to limitation (f)), arguing that those reasons apply to limitation (i) based on nothing

more than the cryptic and conclusory statement (“since the resultant risk map(s) were merely applications of known mathematical calculations to PSMA-binding agent-measured uptake within an identified 3D boundary, e.g., the prostate or, specifically, a prostate tumor. Ex1002, ¶¶185-190.”). Pet. 41-42.

If anything, the Petition’s multiple, distinct, limitation-specific arguments reflect the non-obviousness of the claimed invention. At no point does the Petition step back to consider both the claims and the art as a whole, as is required under 35 U.S.C. § 103. The Petition thus fails to present a coherent and particularized argument as to why a POSA would have the required motivation to combine three distinct references to arrive at Patent Owner’s claimed subject matter.

Third, even to the extent one can follow the Petition’s scattered treatment, the Petition fails to show a reasonable likelihood that a POSA would have been motivated to combine Maier and Huang to perform limitation (f) of claim 1. The Petition contends that “a POSITA would have found it obvious, with a reasonable expectation of success, to incorporate Huang’s fused PET/CT imaging into the system and method of Maier.” Pet., 27-28. Not so. Maier and Huang are simply too different for a POSA to have been motivated to combine them with a reasonable expectation of success. EX2014, ¶94.

The differences are striking. Maier focuses primarily on analysis of CT (or MRI) images to determine “imaging biomarkers” that correlate with various

smoking-related diseases, like “myocardial infarction, Chronic Obstructive Pulmonary Disease (COPD), emphysema, lung cancer, decreased lung function, COPD exacerbations, coronary artery disease, and stroke.” EX1005, [0007]; EX2014, ¶95. Maier repeatedly explains that imaging biomarkers are characteristic patterns in images that are correlated with disease (again, focusing on smoking related diseases):

By way of example, but not limitation, these imaging biomarkers may be: characteristic patterns of intensity values (e.g., percentage or volume of voxels below or above a threshold value, mean image intensity below or above a threshold value, skew of a histogram of image voxel intensities, value for a certain percentile of the image voxel intensity histogram, etc.), image textures (e.g., reticular pattern, honeycomb pattern, ground glass opacities, etc. on CT lung images) ...

EX1005, [0031]. Huang, in contrast, focuses on CAD tools for segmenting hotspots in FDG PET-CT images. EX1006, [0003], [0006], [0051], [0098], [0108]; EX2014, ¶96. Whereas Maier analyzes single CT images to detect characteristic patterns that might correlate with lung disease, Huang’s analysis centers around the fact that tumors appear as bright spots in FDG-PET images. EX2014, ¶96. It is not even clear how Maier could be applied to a PET/CT image, or how Maier’s approach of using machine learning to assign risk to imaging biomarkers would yield predictable results for a PET/CT image. *See id.* Accordingly, Maier’s complicated correlations and various flavors of imaging biomarkers would be irrelevant in Huang. *See id.* It is not clear how, if at all, Huang’s FDG-PET imaging approach would even allow

for assessing risk of all varieties of lung disease, including emphysema, etc. EX2014, ¶96; *see also id.*, ¶¶97, 99. The Petition never attempts to address these key distinctions and incompatibilities between Maier and Huang.

Ultimately, then, the Petition’s motivation to combine argument fails because it ignores the fundamental incompatibilities between Maier and Huang. EX2014, ¶98. The Petition cannot satisfy its burden by simply noting that both Maier and Huang are directed to diagnostics and that Huang says PET/CT imaging is useful. EX2014, ¶98; *supra*, 25. Institution should thus be denied. *See* EX2014, ¶100.

Since this same limitation appears in independent claim 18, the Petition also fails to carry its burden to show that a POSA would have had a motivation to combine Maier and Huang to achieve this same limitation in independent claim 18. The Petition thus also fails to carry its burden for claim 18. EX2014, ¶¶123-124.

2. Maier, Huang, and Armor do not render obvious the use of a “PSMA binding agent” as recited in claims 1 and 18.

Limitation (g) of claim 1 is directed to “generat[ing] a radiologist report for the particular patient according to the one or more medical images for the patient, wherein the one or more medical comprise a CT scan overlaid with a nuclear medicine image obtained at a substantially same time as the CT scan and following administration to the patient of an imaging agent **comprising a Prostate Specific Membrane Agent (PSMA) binding agent . . .**” Pet., 30 (emphasis added); EX2014, ¶101; claim 18 (similar).

Institution should be denied because the Petition fails to show that Maier and Huang render obvious the claimed use of a “PSMA binding agent.” EX2014, ¶¶102-103. The Petition conclusorily argues that “Maier and Huang disclose administering a radiolabeled imaging agent to the patient,” citing in footnotes to “fluorine-18 deoxyglucose (“FDG”)” and “an imaging biomarker such as a functional imaging agent.” Pet., 30-31 (citing EX1005, [0003]-[0005]). The Petition’s argument fails for at least four reasons. EX2014, ¶¶102-103.

First, Maier does not disclose *any* radiolabeled imaging agent, let alone an agent specifically directed to prostate cancer (like PSMA binding agent). EX2014, ¶104. The cited passage in Maier does not even reference a “functional imaging agent,” as the Petition’s quoted footnote contends. *Id.* Instead, the cited passage describes an imaging biomarker as some kind of pattern or feature that one can calculate from an image. EX1005, [0031] (“By way of example, but not limitation, these imaging biomarkers may be: characteristic patterns of intensity values . . . , image textures . . . , dimensions or amount of an anatomical feature . . . , other measurable characteristics of anatomical features . . . , or physiological metrics derived from functional imaging exams . . .”); EX2014, ¶104. The only mention of an “agent” in this laundry list of “imaging biomarkers” in Maier is “metrics related to contrast agent uptake in MR or CT in tumors, or other vascularized tissues, etc.” EX2014, ¶104. A metric related to a contrast agent is not a radiolabeled imaging

agent. *See id.* Moreover, MR and CT images are not nuclear medicine images, and therefore do not use radiolabeled imaging agents. *See id.* Thus, Maier does not even disclose the use of a radiolabeled imaging agent.

Second, Huang does not even mention the prostate or prostate cancer, let alone the idea of radiolabeled agents like PSMA that target specific types of cancer. EX2014, ¶105. Huang describes FDG, which is a generic imaging agent specific to PET imaging. EX1006, [0003]; EX2014, ¶105. Huang describes FDG as a glucose analogue that is absorbed preferentially by tissue with high metabolic activity, and which is not specific to any cancer type. EX1006, [0098]; EX2014, ¶105. In contrast, PSMA binding agents expressly bind to prostate-specific membrane antigen, a protein that is overexpressed in prostate cancer. EX2014, ¶¶105-106. FDG thus operates in a fundamentally different way than a PSMA binding agent: FDG is non-specific, whereas PSMA expressly targets prostate cancer. EX2014, ¶107. Therefore, Huang is inapposite.

Third, although Armor describes the use of a PSMA binding agent, Armor is necessarily incompatible with Maier-Huang. EX2014, ¶108. The Petition argues that Armor supplies the reference to a PSMA binding agent that is missing from Maier-Huang. Pet., 32-33 (“A POSITA could have predictably substituted Armor’s PSMA-binding agents into the Maier-Huang combination to predictably arrive at this claim limitation.”). The Petition’s argument fails, though, because (as discussed

above) Armor and Maier-Huang relate to fundamentally different imaging methods. Huang, as discussed above, involves the use of FDG, which is specific to PET imaging. *See* EX2014, ¶¶32-35. Armor's PSMA binding agent, on the other hand, only works for SPECT imaging. EX2014, ¶108; *see also id.*, ¶¶32-35, 109. PET and SPECT detect different kinds of radiation, and thus require different types of radionuclides. EX2014, ¶108, *see also id.*, ¶¶32-35. Therefore, a POSA would know that they could not simply substitute Armor's SPECT-specific compounds for FDG, since that would result in a non-functioning system. EX2014, ¶108; *see also id.*, ¶109.

Fourth, apart from disclosing PSMA binding agents, Armor is otherwise directed to a wholly conventional imaging technique, and it is not clear from the Petition why a POSA would seek to combine Armor with Huang. EX2014, ¶110. Armor describes image analysis that relies on users (e.g., physicians) to manually mark circular regions of interest on images. *See* EX1007, [0096]; EX2014, ¶110. Armor does not contemplate the shortcomings of a manual image analysis approach, let alone the particular shortcomings in situations where images are repeatedly obtained and analyzed over the course of multiple visits (which is where the '035 Patent's insights into combining automated machine learning-based analysis with cloud-based systems are especially powerful). EX2014, ¶110. Neither Maier nor Huang appears to appreciate this point. *Id.* The Petition appears to take for granted

that Armor would be combined in such a “network-based . . . system” as recited in claim 1 and described in the ’035 Patent. The Petition thus glosses over the fact that Armor appears directed to conventional workstations, in contrast with the ’035 Patent’s network-based approach that includes databases of patient image data to facilitate monitoring patient’s cancer. As explained above, these terms (e.g., “network-based . . . system” and “database”) have particular constructions and, among other things, combine with other elements that work together to provide a comprehensive solution for physicians to diagnose, monitor, and evaluate treatment efficacy for cancer patients. *Supra*, Section VI.

Thus, for at least this reason combination of Maier, Huang, and Armor fails to render claim 1 obvious. EX2014, ¶111.

Since this same limitation appears in limitation (f) of independent claim 18, the Petition also fails to carry its burden to show that a POSA would have had a motivation to combine Maier and Huang to achieve this same limitation in independent claim 18. EX2014, ¶¶123-124. The Petition thus also fails to carry its burden for claim 18.

3. Maier and Huang do not disclose or render obvious “using the composite image to geographically identify . . .” as recited in claims 1 and 18.

Limitation (h) of claim 1 is directed to **“using the composite image to geographically identify a 3D boundary for each of one or more regions of imaged**

tissue within the nuclear medicine image[.]” Pet., 33; EX2014, ¶112; claim 18 (similar). The Petition argues that Maier and Huang render this limitation obvious because “Maier teaches that its processor analyzes medical images,” and “while Maier does not teach automatic analysis of a composite image, Huang teaches this, and a POSITA would have found it obvious to combine these references to arrive at this claim limitation.” Pet., 34; EX2014, ¶113. However, for at least three reasons, the Petition fails to establish that a POSA would have been motivated to combine Maier and Huang with a reasonable expectation of success. EX2014, ¶113.

First, contrary to the Petition’s contention, Huang does not disclose this limitation. EX2014, ¶114. The Petition claims that “Huang trains ‘discriminative classifiers and detectors’ to analyze [CT, PET, and composite PET/CT] images, including creating ‘3D bounding boxes’ of organs.” Pet., 31-32. But Huang’s “discriminative classifiers” do not segment organs and do not identify a 3D boundary for tissue regions. *Id.* Instead, Huang’s classifiers are binary – they take an entire image (which may be a rectangular patch of a larger image) as input and classifies the input image as either (i) a positive example of the landmark (i.e., the landmark is in the image) or (ii) a negative example of the landmark (i.e., the landmark is not in the image). *Id.*; EX1006, [0065], [0066], [0069], [0071], and [0072]. Huang’s “bounding boxes” are just the boundaries of a rectangular patch that was classified as containing a given landmark (essentially any anatomical point or structure of

interest). EX2014, ¶114. That is not segmentation and a bounding box is not a 3D boundary of a tissue region. *See id.*, ¶¶114, 36. Segmentation requires determining a 3D boundary - i.e., a complex outline - of a given organ or bone. *Id.* Thus, contrary to the Petition's contention, Huang does not even disclose this limitation of claim 1.

Second, as discussed above, Huang and Maier disclose fundamentally different solutions to fundamentally different types of imaging. *Supra*, 24-25; EX2014, ¶115. The Petition argues that Huang provides “[i]mproved, organ-specific identification,” but fails to explain why a POSA would be motivated to combine Huang with Maier notwithstanding that Huang focuses entirely on FDG imaging, unlike Maier. Pet., 35; EX2014, ¶115. The Petition's only attempt at emphasizing overlap between Huang and Maier is to note that both use machine learning algorithms, but the Petition cannot carry its burden to show motivation to combine by simply noting that both Maier and Huang sometimes use machine learning. *See* Pet., 35; EX2014, ¶115. The Petition's argument thus fails. EX2014, ¶115.

Third, the Petition does not explain why a POSA would have a reasonable expectation of success in combining Huang and Maier. EX2014, ¶116. The Petition argues that a POSA would have reasonably expected success because “Huang teaches that its system which automatically identifies hotspots is ‘fast (real time), robust and accurate, and can be used as a practical application on a regular basis for

hot-spot detection, segmentation, and change quantification’ in fused PET/CT or SPECT/CT images.” Pet., 37; EX2014, ¶116. This conclusory assertion—unsupported by any other argument—is insufficient. EX2014, ¶116. The question is whether a POSA would have had a reasonable expectation of success in combining the two very different references—not whether Huang considered its own invention to be fast and accurate. *See id.* The Petition thus fails to establish a motivation to combine Huang and Maier to perform limitation (h). *See id.*

Since this same limitation appears in limitation (h) of independent claim 18, the Petition also fails to carry its burden to show that a POSA would have had a motivation to combine Maier and Huang to achieve this same limitation in independent claim 18. The Petition thus also fails to carry its burden for claim 18. EX2014, ¶123-124.

4. **Maier, Huang, and Armor do not disclose or render obvious “computing, using the nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s) a risk map comprising a graphical denotation marking a region of risk of cancer or risk of recurrence of cancer” as recited in claims 1 and 18.**

Limitation (i) of claim 1 is directed to “computing, using the nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s) a risk map comprising a graphical denotation marking a region of risk of cancer or risk of recurrence of cancer.” Pet., 37; EX2014, ¶117; claim 18 (similar). The Petition argues that Maier and Huang render this limitation obvious because “Maier discloses

computing a ‘risk map’” and, “while Maier does not teach computation using a composite image, Huang teaches this[.]” Pet., 38; EX2014, ¶117. The Petition’s argument fails for two reasons.

First, Maier does not disclose computing a risk map. EX2014, ¶118. In support of its assertion to the contrary, the Petition contends that section [0007] (and Figs. 1 and 3) of “Maier calculates, and generates a report which includes, regions of risk related to ‘emphysema, lung cancer, decreased lung function,’ and others.” Pet., 38; EX2014, ¶118. From this, the Petition concludes that Maier thus discloses computing a risk map. Not true. The full quote from [0007] makes this clear: “In some embodiments, the **quantitative health status and risk metrics** may be related to one or any combination of: myocardial infarction, Chronic Obstructive Pulmonary Disease (COPD), emphysema, lung cancer, decreased lung function, COPD exacerbations, coronary artery disease, and stroke.” EX1005, [0007] (emphasis added); EX2014, ¶118. The same issue applies to Figure 1. Nowhere does Maier disclose computing 3D regional boundaries to form a risk map. *See id.*

Fig. 3 of Maier also fails to disclose a risk map. EX2014, ¶119. As recited in claim 1, a risk map comprises “a graphical denotation marking a region of risk of cancer or risk of recurrence of cancer.” EX1001, 36:51-52; EX2014, ¶119. Maier describes Fig. 3, however, as showing how “the lung image is re-colored to fit a lay person's conception of lung health with the normal portion of their lungs shown as

pink to indicate normal tissue, and the **likely emphysema** portion of the lungs shown as black to indicate a diseased state, and an outline of a torso is shown surrounding the lung in order to provide a reference for the patient to their own anatomy.” EX1005, [0026] (emphasis added); EX2014, ¶119. Emphysema is not cancer, and thus Maier does not disclose computing a risk map for the purpose taught in the claims of the ’035 Patent. EX2014, ¶119.

Second, to the extent the Petition argues that Huang discloses the risk map, the Petition fails to carry its burden to explain why a POSA would have been motivated to combine Huang’s risk map with Maier. EX2014, ¶120. The Petition conclusorily argues that “the resultant risk map(s) were merely applications of known mathematical calculations to PSMA-binding agent-measured uptake within an identified 3D boundary, e.g., the prostate or, specifically, a prostate tumor.” Pet., 40-41; EX2014, ¶120. This unsupported assertion is insufficient to carry the Petition’s burden. EX2014, ¶120.

Therefore, the Petition fails to show that a POSA would have been motivated to combine Maier and Huang to perform limitation (i) because the Petition does not address how or why one would be motivated to combine (a) Maier, who analyzes CT images to detect emphysema, with (b) Huang, who creates CAD tools for FDG-PET images to detect tumors (but does not mention any specific cancer type and does not even mention the prostate), and with (c) Armor, who is directed to PSMA

binding agents for SPECT-CT imaging (which are incompatible with PET). EX2014, ¶121.

Since this same limitation appears in limitation (i) of independent claim 18, the Petition also fails to carry its burden to show that a POSA would have had a motivation to combine Maier and Huang to achieve this same limitation in independent claim 18. EX2014, ¶¶123-124. The Petition thus also fails to carry its burden for claim 18. *See id.*

Because, for at least the reasons explained above, the Petition fails to show that independent claims 1 and 18 are rendered obvious under Ground A, the Petition's arguments under Ground A also fail with regard to (i) dependent claims 2-7 and 9-17, which depend from claim 1 and (ii) dependent claims 19-24 and 26-35, which depend from claim 18. EX2014, ¶125.

B. Ground B: Maier in view of Huang and Armor, in further view of Neumaier does not render obvious claims 5-8 or 22-25.

For Ground B, the Petition only alleges that Neumaier discloses “a PSMA targeted radiotracer to diagnose prostate cancer and its progression”, but otherwise relies on Maier, Huang, and Armor for every other element of claims 5-8 and 22-25. Pet., 58; EX2014, ¶126. The Petition does not contend that Neumaier discloses any other limitations of those claims. EX2014, ¶126. Accordingly, for at least the reasons above, Maier, Huang, Armor, and Neumaier fail to render claims 5-8 and 22-25 obvious. *See id.*

C. Ground C: Huang in view of Armor does not render obvious claims 36 or 41.

1. Huang and Armor do not disclose or render obvious “repeatedly receiving and storing in a database” as recited in claims 36 and 41.

Limitation (a) of claim 36 is directed to “repeatedly receiving and storing **in a database**, over time, by a processor of a computing device, a plurality of medical images . . .” Pet., 63 (claim 36); claim 41 (similar); EX2014, ¶127. The Petition argues that Huang renders this limitation obvious because “Huang teaches that its method is performed by a processor of a computing device,” including “a central processing unit (CPU) 192” and “a memory 193 . . .” Pet., 63-64; EX2014, ¶127.

The Petition’s argument fails because Huang does not disclose the use a “database” to “repeatedly receiv[e] and store[]” medical images. Pet., 63 (claim 36); 68 (claim 41). EX2014, ¶128. The Petition does not even argue otherwise. Pet., 63-64. As explained above, a processor is not a database, and a memory is not a database. *Supra*, 14-17; EX2014, ¶¶86-87. Therefore, the Petition fails to show that Huang and Armor render this limitation obvious.

2. Huang and Armor do not disclose or render obvious tracking risk indices that are indicative of “prostate cancer state or progression” “over a course [of] prostate cancer progression and treatment,” as recited in claims 36 and 41.

Limitation (b)(2) of claim 36 is directed to “value of one or more risk indices for each medical image of the series, thereby tracking determined values of the one or more **risk indices over a course [of] prostate cancer progression and**

treatment for the patient.” Pet., 65 (claim 36); claim 41 (similar); EX2014, ¶129. The Petition argues that Huang and Armor render this limitation obvious because “this limitation is substantively identical to a combination of claims 15 and 16, addressed in Sections VIII.B.14 and VIII.B.15” in the Petition. Pet., 65; EX2014, ¶130.

The Petition’s argument fails for two reasons. First, the two cross-referenced sections (VIII.B.14-15) recite arguments based on a different combination of references (*Maier*, Huang, and Armor). It is therefore unclear how those arguments apply to a combination of only Huang and Armor. EX2014, ¶131. Second, neither claim 15 nor claim 16 recites a risk index “indicative of **prostate cancer state** or progression,” as recited in this claim, nor do they recite “tracking determined values of the one or more risk indices **over a course [of] prostate cancer progression and treatment for the patient.**” EX2014, ¶132; *see, e.g.*, EX1001, 37:14-16 (claim 15, reciting “compute a value of each of one or more risk indices, each risk index value indicative of **cancer state** or progression in the patient,”), 37:23-24 (claim 16, reciting “tracking determined values of at least the first risk index for the first patient **over time.**”). Prostate cancer is a specific type of cancer, and “over a course [of] prostate cancer progression and treatment,” is a specific range of time. The Petition does not acknowledge this additional specificity in claims 36 and 41 and thus fails to explain how those elements are disclosed in the cited art. EX2014, ¶132.

Therefore, the Petition fails to show that Huang and Armor render this limitation obvious. EX2014, ¶132.

3. Huang and Armor do not render obvious “a Prostate Specific Membrane Antigen (PSMA) binding agent . . .” as recited in claims 36 and 41.

Limitation (e) of claim 36 is directed to “and following administration to the patient of an imaging agent comprising a **Prostate Specific Membrane Agent (PSMA) binding agent** comprising a radionuclide . . .” Pet., 67 (claim 36); claim 41 (similar); EX2014, ¶133. The Petition argues that Huang and Armor render this limitation obvious because “this limitation is substantively identical to limitation [1(g)], addressed in Sections VIII.B.1.h” in the Petition. *Id.*, 67; EX2014, ¶134.

As explained above, the Petition fails to show that a POSA would have been motivated to combine Huang and Armor to achieve the claimed limitation with a reasonable expectation of success. EX2014, ¶135.

4. Huang and Armor do not disclose or render obvious “geographically identifying a 3D boundary for each of one or more regions of imaged tissue . . .” as recited in claims 36 and 41.

Limitation (f) of claim 36 is directed to “using the composite image to **geographically identify a 3D boundary** for each of one or more regions of imaged tissue within the corresponding nuclear medicine image . . .” Pet., 68 (claim 36); claim 41 (similar); EX2014, ¶136. The Petition argues that Huang and Armor render this limitation obvious because “this limitation is substantively identical to limitation

[1(h)], addressed in Sections VIII.B.1.i” in the Petition. *Id.*, 68; EX2014, ¶137. In that section, the Petition argues that “Huang trains ‘discriminative classifiers and detectors’” to analyze CT, PET, and composite CT/PET images. Pet., 34; EX2014, ¶137.

The Petition’s argument fails at least because, as explained above, Huang’s “discriminative classifiers and detectors” do not segment organs and do not identify a 3D boundary for tissue regions. EX2014, ¶138. Instead, they are, as Huang states, “classifiers” – they label an entire rectangular image patch (e.g., with a 1 or a 0 for an entire rectangular patch) according to whether it contains a given landmark or not. *Id.* That is not segmentation, which requires determining a 3D boundary - i.e., a complex outline - of a given organ or bone. *See id.* As such, Huang’s classifier does not perform segmentation, nor does it “geographically identify . . .,” as recited in claim 36. EX2014, ¶138. The Petition thus fails to show that Huang and Armor render this limitation obvious. EX2014, ¶138.

5. **Huang and Armor do not disclose or render obvious “using the corresponding nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s) to compute (i) the value of each of the one or more risk indices and (ii) the risk map” as recited in claims 36 and 41.**

Limitation (g) of claim 36 is directed to “using the corresponding nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s) to compute (i) the value of each of the one or more risk indices and (ii) the risk map.” Pet., 68 (claim 36); claim 41 (similar); EX2014, ¶139. The Petition argues that Huang and Armor render this limitation obvious because “this limitation is substantively identical to limitation [1(i)] of claim 15, addressed in Sections VIII.B.1.j and VIII.B.14” in the Petition. Pet., 68; EX2014, ¶140.

The Petition’s argument fails, however, because the two cross-referenced sections recite arguments based on a different combination of references (*Maier*, Huang, and Armor). EX2014, ¶141. It is therefore unclear how those arguments apply to a combination of only Huang and Armor. *See id.* The Petition thus fails to show that Huang and Armor render this limitation obvious. *See id.*

VIII. CONCLUSION

For all the foregoing reasons, the Board should deny institution of the Petition.

Date: July 14, 2025

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CERTIFICATION UNDER 37 C.F.R. § 42.24(d)

I hereby certify that the foregoing complies with the type-volume limitation of 37 C.F.R. § 42.24 and contains 9,483 words based on the word count indicated by the word-processing system used to prepare the paper, excluding the table of contents, table of authorities, mandatory notices under 37 C.F.R. § 42.8, certificate of service, certificate of word count, appendix of exhibits, signature block, and claim listing.

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing **PATENT OWNER'S PRELIMINARY RESPONSE** was served electronically in its entirety on July 14, 2025 via electronic mail to the following attorneys of record:

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