

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Fujirebio Diagnostics, Inc.
Petitioner,

v.

Quanterix Corp.
Patent Owner.

U.S. Patent No. 11,275,092
Issue Date: March 15, 2022

Title:
Methods of determining a treatment protocol for
and/or a prognosis of a patient's recovery from a brain injury

Inter Partes Review No.: IPR2025-01060

**PETITIONER'S OPPOSITION TO PATENT OWNER'S
REQUEST FOR DISCRETIONARY DENIAL OF INSTITUTION**

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U.S. Patent and Trademark Office
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Petitioner's Exhibit List

<i>Exhibit #</i>	<i>Description</i>
1001	U.S. Patent No. 11,275,092 ("the '092 Patent")
1002	Select portions of prosecution history of the '092 Patent, i.e., select portions of the file history of US application No. 16/522,237 ("File History")
1003	Declaration of Petitioner's Expert John Todd, PhD ("Todd Dec")
1004	Curriculum vitae of Petitioner's Expert John Todd, PhD
1005	Rissin et al., Single-molecule enzyme-linked immunosorbent assay detects serum proteins at subfemtomolar concentrations. Nat Biotechnol. 28(6):595-9 and Supplementary information (4 pages) available at https://static-content.springer.com/esm/art%3A10.1038%2Fnbt.1641/MediaObjects/41587_2010_BFnbt1641_MOESM21_ESM.pdf (Epub May 23, 2010) ("Rissin")
1006	John Todd, et al., How Low Can You Go? Next generation immunoassay systems and the revival of protein biomarkers. Drug Discovery World, Fall 2008 ("Todd") available at https://www.ddw-online.com/media/32/fall-08-immunoassay-systems.pdf . ("Todd")
1007	Voorheis, "Diagnostic Method For Alzheimer's Disease By Screening For Tau-Peptides in the Blood of a Patient", US Patent No. 5,492,812 ("Voorheis")
1008	File History of US application No. 08/159,969, filed November 30, 1993, which matured into US Patent No. 5,492,812 (Voorheis, EX-1011), and published February 20, 1996 with the issuance of Voorheis, EX-1007 ("Voorheis FH") (An electronic copy (pdf) is supplied with the filing of this Petition, and Petitioner also has a Certified Copy of Voorheis FH from the National Archives, available for filing by hand with the Board)
1009	Rissin & Walt, "Digital Concentration Readout of Single Enzyme Molecules Using Femtoliter Arrays and Poisson Statistics", Nano Lett. 6(3): 520-523 (2006) ("Rissin 2006")
1010	Rissin et al., "Simultaneous Detection of Single Molecules and Singulated Ensembles of Molecules Enable Immunoassays with Broad Dynamic Range", Anal. Chem. 83:2279-2285 (2011) ("Rissin 2011")

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1011	Bourzac, “Next-Generation Diagnostics A startup can detect tiny traces of cancer markers in blood samples”, MIT Technology Review, May 13, 2008, available at: https://www.technologyreview.com/2008/05/13/220548/next-generation-diagnostics/
1012	Todd et al., “Ultrasensitive Flow-based Immunoassays Using Single-Molecule Counting”, Clinical Chemistry 53(11):1990-1995 (2007) (“Todd 2007”)
1013	Nam et al., “Nanoparticle-Based Bio-Bar Codes for the Ultrasensitive Detection of Proteins, Science 301: 1884-1886 (2003) (“Nam”)
1014	Thaxton et al., “Nanoparticle-based bio-barcode assay redefines ‘undetectable’ PSA and biochemical recurrence after radial prostatectomy”, PNAS 44:18437-18442 (2009)
1015	Duffy et al., US2010/0075407 (“the ’407 publication” or “Duffy”), published March 25, 2010
1016	Rissin et al., “Digital Readout of Target Binding with Attomole Detection Limits via Enzyme Amplification in Femtoliter Arrays”, JACS Communications 19(128) 6286-6287 (2006) (“Rissin 2006a”)
1017	Wunderlich et al., “Neuron-specific enolase and tau protein as neurobiochemical markers of neuronal damage are related to early clinical course and long-term outcome in acute ischemic stroke”, Clinical Neurology and Neurosurgery 108:558-63 (Sep. 2006) (“Wunderlich”)
1018	Mortberg, “Assessment of the Cerebral Ischemic/Reperfusion Injury after Cardiac Arrest”, Acta Universitatis Upsaliensis Uppsala. Dissertation, 71 pages (2010) (“Mortberg”)
1019	Ding et al., Transl Neurodegener 10:10 (2021). https://doi.org/10.1186/s40035-021-00234-5 (“Ding”)
1020	Medeiros, et al., “The Role of Tau in Alzheimer’s Disease and Related Disorders”, CNS Neuroscience & Therapeutics 17: 514–524 (2011) (“Medeiros”)
1021	Weingarten et al., “A protein factor essential for microtubule assembly”, PNAS 72:1858-1862 (1975) (“Weingarten”)
1022	Konzack et a., “Swimming against the Tide: Mobility of the Microtubule Associated Protein Tau in Neurons”, J Neuroscience 27(37):9916 –99271 (2007)
1023	Vanmechelen et al., “Differential Diagnosis of Neurological Diseases”, US Patent No. 6,670,137 (“Vanmechelen”)

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1024	April 9, 2004 “INNOTEST hTAU Ag” webpage of Innogenetics downloaded from “Wayback Machine”, https://web.archive.org/web/20040914040003fw/http://www.innogenetics.be/site/prodview.asp?id=38&lang=E&print=true , accessed January 11, 2025 (“INNOTEST”)
1025	Galasko, “Biomarkers for Alzheimer’s disease – Clinical needs and application”, J Alzheimer’s Disease 8:339-346 (2005) (“Galasko”)
1026	Vandermeeren et al., “Detection of τ Proteins in Normal and Alzheimer’s Disease Cerebrospinal Fluid with a Sensitive Sandwich Enzyme-Linked Immunosorbent Assay”, J Neurochem. 61:1828-1834 (1993) (“Vandermeeren”)
1027	Hulstaert et al. / Innogenetics N.V., “Tau as a Marker for Early CNS Damage”, WO00/14546 (March 16, 2000) (“Hulstaert”)
1028	Vandermeeren et al., “Monoclonal Antibodies Directed Against the Microtubule-Associated Protein Tau, and Hybridomas Secreting These Antibodies”, US Patent No. 5,843,779, issued December 1, 1998 (“Vandermeeren ’779”)
1029	de Jong, et al., “Current state and future directions of neurochemical biomarkers for Alzheimer’s disease” Clin. Chem. Lab. Med. 45: 1421–1434, 1424-25 (2007)
1030	May 29, 2010 Screenshot of “Alzheimer’s Disease” webpage of Quanterix downloaded from “Wayback Machine”, https://web.archive.org/web/20100529185326/http://www.quanterix.com/applications/ad.html , accessed January 7, 2025 (“PO Website May 29, 2010”)
1031	Schraen-Maschke et al., “Tau as a biomarker of neurodegenerative diseases”, Biomark Med 2(4): 363-384 (2008) (“Schraen-Maschke”)
1032	Blennow et al., CSF markers for incipient Alzheimer’s disease”, Lancet Neurol 2(10):605-13 (2003) (“Blennow”)
1033	Quanterix Single Molecule Arrays for Digital Detection in Complex Samples, IQT Technology Focus Day, March 25, 2010 presentation (“Quanterix Presentation”)
1034	October 22, 2013 Screenshot “simoa Assay Kits” webpage of Quanterix downloaded from “Wayback Machine”, https://web.archive.org/web/20131022204103/http://quanterix.com/products/assay-kits , accessed May 27, 2025 (showing Tau Simoa Assay commercially available) (“PO Website Oct 22, 2013”)

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1035	Nalefski, <i>et al.</i> , “Single-Molecule Detection for Femtomolar Quantification of Proteins in Heterogeneous Immunoassays”, <i>Clinical Chemistry</i> 52(11): 2172–2175 (1 November 2006), https://doi.org/10.1373/clinchem.2006.072850 and DOI: 10.1373/clinchem.2006.072850
1036	September 12, 2009 Screenshot “Singulex [®] Assay Menu Erenna [®] Immunoassay System”, A β -42 (Amyloid beta protein 42) webpage of Singulex, Inc. downloaded from “Wayback Machine”, https://web.archive.org/web/20090912044340/http://www.singulex.com:80/assay_details.html?id=2 , accessed April 24, 2025 (“Singulex Website Aug. 12, 2009”)
1037	Gavett BE, <i>et al.</i> : “Mild traumatic brain injury: a risk factor for neurodegeneration.” <i>Alzheimer’s Research & Therapy</i> 2010, 2:18, doi:10.1186/alzrt42
1038	Mortimer JA, <i>et al.</i> : “Head trauma as a risk factor for Alzheimer’s disease: a collaborative re-analysis of case–control studies.” EURODEM Risk Factors Research Group. <i>Int J Epidemiol</i> 1991, 20:S28-S35.
1039	Quanterix July 30, 2013 Press Release “Quanterix Announces Commercial Availability of its Simoa Single Molecule Array Technology”, available at, https://www.quanterix.com/wp-content/uploads/2020/12/Simoa_7-30-13_FINAL-Press-Release.pdf , accessed May 28, 2025 (“Quanterix 7/30/13 Press Release”)
1040	Quanterix August 7, 2012 Press Release “Quanterix Issued Key Patent for Simoa [™] Technology”, available at, https://www.biospace.com/quanterix-issued-key-patent-for-simoa-and-0153-technology , accessed May 28, 2025 (“Quanterix 8/17/12 Press Release”)
1041	Quanterix October 16, 2013 Press Release “Quanterix Announces Key Patents Issued for Simoa Platform”, available at, https://www.quanterix.com/wp-content/uploads/2020/12/Patents_Release_FINAL.pdf , accessed May 28, 2025 (“Quanterix 10/16/13 Press Release”)
1042	Bogoslovsky et al., “Increases of Plasma Levels of Glial Fibrillary Acidic Protein, Tau, and Amyloid β up to 90 Days after Traumatic Brain Injury”, <i>J Neurotrauma</i> 34:66–73 (2017) (citation 28 of Ding) (“Bogoslovsky”)

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1043	Declaration of Ingrid Hsieh-Yee
1044	Select portions of the prosecution history of the US application No. 15/269,142 (“142 File History”)
1045	Select portions of the prosecution history of the US application No. 14/111,326 (“326 File History”)
1046	U.S. Food & Drug. Administration May 16, 2025 News Release “FDA Clears First Blood Test Used in Diagnosing Alzheimer’s Disease”, available at https://www.fda.gov/news-events/press-announcements/fda-clears-first-blood-test-used-diagnosing-alzheimers-disease , accessed September 17, 2025 (“FDA 5/16/25 News Release”)

I. INTRODUCTION

The Director should deny Patent Owner's Request for Discretionary Denial under 35 U.S.C. §§ 325(d) and 314(a).

Discretionary denial under § 325(d) is not appropriate in this case because neither prong of the *Advanced Bionics* framework is satisfied. First, neither the combinations of prior art in the asserted grounds, nor the arguments raised in the Petition¹, were previously presented to the Office. Indeed, Todd (EX-1006) was not before the Examiner during original prosecution. And second, the Examiner materially erred by:

- not uncovering Todd in searching and examining the '092 Patent;
- overlooking the teachings of Rissin (EX-1005) (which had been buried by in an IDS with 616 other references and not used as a basis for a §103 rejection or otherwise discussed or acknowledged during prosecution of the challenged patent);
- not rejecting the claims as obvious over Rissin in view of the Todd and Voorheis (EX-1007) references as asserted in the Petition;

¹ Petition for Inter Partes Review of U.S. Patent No. 11,275,092, *Fujirebio Diagnostics, Inc. v. Quanterix Corp.*, No. IPR2025-01060 (P.T.A.B. May 28, 2025), Paper No. 2 (the "Petition").

- interpreting the claim scope as limited to “tau Simoa” (Reasons For Allowance, EX-1002, 659-60);
- misinterpreting Ding (EX-1019) (Reasons For Allowance, EX-1002, 659-60); and
- withdrawing § 103 rejections without any evidentiary basis therefor, especially as the case of obviousness against the '092 claims is so strong that no assertions of secondary considerations, even if presented by way of declaration or affidavit, can overcome the obviousness; *see* MPEP 2145 (citing *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007); *Leapfrog Enters Inc. v. Fisher-Price Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007); *Newell Cos., Inc. v. Kenny Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988))..

Moreover, the Patent Owner urged the Examiner to make the above material errors by misrepresenting the closest prior art and the state of the art during prosecution. It would be manifestly unfair to allow the Patent Owner to benefit again from its misrepresentation by discretionarily denying review and avoiding consideration of the claims based on the closest prior art.

Discretionary denial under § 314(a) is likewise not appropriate in this case for several reasons.

First, the co-pending litigation in the District of Delaware is in its nascent stages. Issue has not been met, and if the Delaware litigation proceeds beyond pre-Answer motions, it is not expected that issue will be met until sometime in 2026.² Thus, no scheduling order has been entered, no trial date has been set, and median time-to-trial statistics and other evidence shows that any possible future trial would likely occur well after the December, 2026 statutory deadline for a final written decision in this IPR.

² On September 5, 2025, counterclaim defendants, Fujirebio Diagnostics, Inc. (“FDI”) and Fujirebio Europe N.V. (“FRE”), each filed a motion to dismiss under Fed. R. Civ. P. 12(b)(6). FRE is a separate legal entity from FDI, and is **not** the Petitioner in this IPR. Nor is FRE a parent or subsidiary of FDI, and FRE does **not** control and is **not** controlled by FDI. While Patent Owner named FRE as a counterclaim defendant in the district court litigation, it failed to allege any specific activities as to FRE and, thus, FRE has moved to dismiss Patent Owner’s infringement claims. FDI has concurrently moved to dismiss Patent Owner’s infringement claims because the ’092 Patent claims patent-ineligible subject matter under 35 U.S.C. § 101. The briefing on those motions will continue into November, with oral argument and a decision on the motions occurring thereafter.

Second, Petitioner has provided to Patent Owner concurrently herewith a *Sotera* stipulation, making clear that, if IPR proceedings are instituted, neither the Petitioner, nor counter-claim defendant FRE, will pursue in the district court proceeding any other ground that was raised, or could have been reasonably raised, in this IPR petition.

Third, the evidence also shows that, if the district court litigation proceeds past the motion to dismiss phase, the district court is likely to grant a stay in the parallel litigation, further alleviating any concerns about inefficiency and duplication of efforts between the district court and the Board.

Finally, other considerations, including the clear strength of the Petition, the absence of any “settled expectations,” and the aim of correcting a material error made by the Office in improvidently issuing claims 1 and 6-21 of the '092 Patent (the “Challenged Claims”), also support institution and weigh against discretionary denial under § 314(a).

Indeed, given that the product at issue is a breakthrough diagnostic test capable of diagnosing Alzheimer's Disease, a devastating and progressive disease, the equities and the public interest strongly favor Board review of dubious patent rights that could prevent such life-saving assays from reaching the market. *See* FDA 5/16/25 News Release, EX-1046.

For at least these reasons and those provided below, Petitioner respectfully requests that the Director reject Patent Owner's request for discretionary denial and allow this IPR to proceed to an institution determination on the merits.

II. THE DIRECTOR SHOULD NOT EXERCISE HER DISCRETION TO DENY INSTITUTION OF THE PETITION

A. Discretionary Denial Under 35 U.S.C. § 325(d) is Not Appropriate

When determining whether to exercise discretion under § 325(d), “the Board uses a two-part framework”: (1) whether the “same or substantially the same” art or arguments previously were presented to the Office; and, if so, (2) “whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.” *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (Feb. 13, 2020) (designated: March 24, 2020) (“*Advanced Bionics*”).

1. *Advanced Bionics* – Step 1 - Neither the Prior Art Combinations Nor the Arguments Raised in the Petition Were Previously Presented to the Office

The first prong of the *Advanced Bionics* framework is not satisfied here as neither the combinations of prior art in the asserted grounds, nor the obviousness arguments raised in the Petition, were previously presented to the Office.

The Petition raises two grounds, each asserting obviousness based on a combination of Rissin (which teaches an ultra-sensitive assay (called a Single Molecule Array or “SiMoA” assay) capable of detecting individual biomarker

molecules in solution) combined with either Todd (Ground 1) or Voorheis (Ground 2), both of which expressly teach the need to and benefits of applying more sensitive diagnostic assays to detect tau protein biomarkers in the blood of patients suspected of having a neurological disorder, such as Alzheimer's disease. *See* Petition, Paper No. 2, at 36-37, 58-61. That is, Rissin teaches the assay; and Todd and Voorheis provide the express motivation for applying that assay to detect tau in patient's blood.

Patent Owner does not dispute that neither of Petitioner's combinations was before the Examiner during prosecution. Rather, at best, two of the three references relied upon in this petition (Rissin and Voorheis) were submitted in a voluminous IDS during prosecution listing references that span more than eight-pages of the patent, EX-1001, pp 1-9. The third reference (Todd) was *never* uncovered by the Examiner, submitted by Patent Owner, or considered by the Examiner at all. Thus, under *Becton, Dickinson* factor (a) there are material differences between the Petition art—*i.e.*, the asserted *combinations* of references that form the asserted grounds—and the prior art involved during examination. These new references and combinations weigh against discretionary denial under part one of the *Advanced Bionics* test.

Unable to satisfy *Becton, Dickinson* factor (a), Patent Owner attempts to lead the Board through a series of false and incomplete comparisons to create the

appearance that Petitioner's grounds are cumulative. First, ignoring arguments made to obtain allowance of the '092 Patent, Patent Owner argues that Petitioner's primary reference, Rissin, was (i) cited during prosecution of an earlier-filed family member application; and (ii) is somehow cumulative of a different reference, Duffy, that was applied during prosecution of the application that issued as the '092 Patent. Next, turning to Petitioner's secondary references, Patent Owner argues that Todd and Voorheis are cumulative of "multiple tau references" also allegedly considered by the Examiner, including "Quanterix 2010a, Mortberg and Wunderlich." By glossing over the arguments Patent Owner made to secure allowance of the claims, Patent Owner argues that both the combination of Rissin in view of Todd, and the combination of Rissin in view of Voorheis, are cumulative of the art that was previously considered. Patent Owner's dismissive attempt at hand waiving, however, is flawed at every step along the way.

As demonstrated below, the Examiner's rejection based on Rissin during prosecution of an earlier family member application was never overcome and, thus, is of little moment to Petitioner's arguments. Nor is Rissin cumulative of Duffy – the reference actually considered by the Examiner during prosecution of the relevant application – as Rissin actually *corrects errors* in the passages in Duffy over which Patent Owner contends Rissin is cumulative. Similarly, neither Todd nor Voorheis are cumulative of other "tau references", as both references supply the motivation to

combine that Patent Owner argued was allegedly “missing” to obtain allowance of the claims. So, not only were neither of the asserted obviousness combinations previously presented to the Office, they expressly address material errors advanced by Patent Owner – and adopted by the Examiner – that secured allowance of the Challenged Claims.

Moreover, the asserted combinations include and are based on new evidence – including the expert declaration of Dr. John Todd explaining the teachings of Rissin, Todd and Voorheis, and why a person of ordinary skill (POSA) would have been motivated, and found it obvious, to make these new combinations of references that were not before the Examiner – including as they involve new art and raise new arguments that were not previously considered. Accordingly, the first prong of the *Advanced Bionics* analysis is not met. *See, e.g., Nikon Corp. v. Optimum Imaging Techs., LLC*, IPR2024-01373, Paper 17 at 28 (P.T.A.B. Apr. 23, 2025) (finding first prong of *Advanced Bionics* not satisfied where same primary reference (Niikawa) had been raised but not considered in a prior IPR but other references in the currently asserted obviousness combinations had not been previously presented); *ETN Cap., LLC v. FBA Operating Co.*, IPR2024-01445, Paper 14 at 14-16 (P.T.A.B. Feb. 28, 2025) (agreeing that “each of the references [petitioner] combine[d] with [a reference before the Office during prosecution] were not considered by the Examiner” and finding that the same or substantially the same art or arguments were

not previously presented to the Office); *Samsung Elecs. Co. v. Maxell, Ltd.*, IPR2024-00906, Paper 11 at 11, 14-18 (P.T.A.B. Dec. 11, 2024) (finding first prong of *Advanced Bionics* was not satisfied where certain references in the asserted obviousness grounds (e.g., Dua) had been listed in an IDS but other references used in combination (e.g., N93, Herle, Rooyen, Desai) were not previously before the Examiner, stating the Board was unpersuaded that “art substantially the same as ***Petitioner's grounds*** were previously presented to the Office” (emphasis added)); *Taro Pharms. U.S.A., Inc. v. Apotex Techs., Inc.*, IPR2017-01446, Paper 7 at 18 (P.T.A.B. Nov. 28, 2017) (declining to exercise discretion to deny Petition based on new expert declaration evidence that was not previously presented to the Office).

2. *Advanced Bionics* – Step 2 - The Examiner Materially Erred by Not Rejecting the Claims as Obvious over Rissin in view of Todd or Voorheis

Although the Director need not reach the second prong of the *Advanced Bionics* framework, it too does not support discretionary denial under § 325(d). The Examiner materially erred by overlooking the teachings of Rissin and by not uncovering Todd during search and examination, and not rejecting the claims as obvious over Rissin in view of Todd or Voorheis. *Advanced Bionics*, IPR2019-01469, Paper 6 at 8 n.9 (“An example of a material error may include misapprehending or overlooking specific teachings of the relevant prior art where those teachings impact patentability of the challenged claims.”); *id.* at 10 (“[I]f the

record of the Office's previous consideration of the art is not well developed or silent, then a petitioner may show the Office erred by overlooking something persuasive[.]").

i. The Examiner's Failure to Consider Rissin in View of Todd Was Material Error

(a) Rissin is Neither Cumulative Of Duffy Nor Before the Examiner

The Examiner never uncovered Todd during search and examination and never considered the obviousness of the Challenged Claims over Rissin in view of Todd. Patent Owner attempts to address this material error by asserting that "Petitioner's resort to Rissin as a primary reference, rather than the Duffy reference cited by the Examiner, is a distinction without a difference." Patent Owner's Brief in Support of Discretionary Denial, *Fujirebio Diagnostics, Inc. v. Quanterix Corp.*, No. IPR2025-01060 (P.T.A.B. Aug. 20, 2025) ("PO DD Brief"), Paper No. 9, at 10. Patent Owner argues that Rissin and Duffy are the essentially the same, and that the Examiner had "cited Rissin and Duffy interchangeably for essentially the same teachings throughout his examination of the applications in the '092 Patent family." *Id.* at 12. Not only is Patent Owner's recitation of the prosecution of the related parent applications less than fulsome, but – in the application that matured into the '092 Patent – Patent Owner expressly overcame the Examiner's rejection applying Duffy based on alleged differences in the claim scope that are *expressly*

taught by Rissin. And despite Patent Owner's intimate knowledge of Rissin – indeed Patent Owner admits that the “authors of Rissin worked for Patent Owner Quanterix and Rissin's author list includes every one of the named inventors of the Duffy reference” – Patent Owner nonetheless failed to alert the Examiner that Rissin disclosed all of the claim limitations that Patent Owner argued purportedly “distinguished” the Challenged Claims from Duffy. *Id.* at 10-11³. Patent Owner's attempts to sweep these differences under the rug by way of a less than complete recitation of the prosecution history should not be rewarded.

³ Patent Owner also did not correct the Examiner's misinterpretation of Ding, or the Examiner's claim interpretation in the Reasons For Allowance, EX-1002, 659-660, or cite and call attention to Patent Owner's May 29, 2010 Website (EX-1030) that explicitly taught diagnosing Alzheimer's Disease “using Quanterix's SiMoA technology, it is now possible to detect these same proteins [that are in CSF] with a simple blood test, even though they are present in blood at exceedingly low concentrations, well below the limit of detection achieved by standard testing methods”, in direct contravention to the arguments advanced by Patent Owner to the Examiner that obtained allowance of the '092 Patent claims.

(b) Patent Owner Never “Overcame” an Obviousness Rejection Over Rissin

Patent Owner's reliance on the prosecution history of related family members to assert that Rissin was previously considered and overcome during examination fails to paint a complete picture of the prosecution. While Patent Owner readily points out that “during prosecution of the earliest patent application in the '092 Patent's family, U.S. Patent Application No. 14/111,326, the same Examiner rejected the pending claims over the combination of Rissin... with Hulstaert... to arrive at the claimed invention...”, Patent Owner tactfully fails to disclose that that rejection was *never overcome* – but rather that the Patent Owner acquiesced in claimed subject matter being obvious in view of Rissin.

More in particular, instead of distinguishing the rejected claims in the parent application (which mirror the scope of the claims challenged in the instant Petition), Patent Owner simply *cancelled them* and then subsequently let the application go abandoned. *See* EX-1045, 869-74 (cancelling rejected claims 1-13 and 20-25 in response to January 29, 2015 Non-Final Office Action); *see also id.* at 5226-31 (responding to subsequent Notice of Non-compliant Amendment by correcting claim numbering presented in response to January 29, 2015 Non-Final Office Action); *id.* at 7994 (issuing Notice of Abandonment in application for failing to respond to March 18, 2016 Non-Final Office Action within the six-month statutory deadline). Thus, contrary to the implication left to be drawn from Patent

Owner's arguments in this IPR, the Examiner never acquiesced to any argument that Rissin did not teach an assay within the scope of the Challenged Claims, or that the combination of Rissin with a secondary reference suggesting measuring tau protein in blood was somehow non-obvious. Rather the Examiner's rejection was left unaddressed, and by claim cancellation it is the Patent Owner who acquiesced in the rejection that the claimed subject matter is obvious in view of Rissin.

Patent Owner's arguments regarding "the next-filed application in the family, U.S. Patent Application No. 15/269,142" are equally misplaced. As Patent Owner tacitly admits, the Examiner "rejected the then-pending claims under § 101" not under §103.⁴ PO DD Brief, Paper No. 9, at 12. That is, the Examiner relied on Rissin only to establish that the routine assay steps in the claimed method

⁴ The determination of lack of an inventive concept under § 101 is separate and apart from considerations of novelty or nonobviousness under 35 U.S.C. §§ 102 and 103. *See Mayo Collaborative Servs. v. Prometheus Lab'ys., Inc.*, 566 U.S. 66, 91 (2012) (rejecting "the Government's invitation to substitute §§ 102, 103, and 112 inquiries for the better established inquiry under § 101"); *see also Intell. Ventures I LLC v. Symantec Corp.*, 838 F.3d 1307, 1315 (Fed. Cir. 2016) (quoting *Diamond v. Diehr*, 450 U.S. 175, 188–89 (1981)).

– *i.e.*, generic instructions to use assays of high sensitivity to detect proteins – was “no more than conventional wisdom in art and... were known and routinely used in this matter.” EX-2002, 5; *see also id.* at 6 (concluding that pending claims “do[] not provide significantly more than instructions to a relevant audience to use known techniques to observe a natural phenomenon and to ‘apply it’. This is not patent eligible.”). As in the earlier U.S. Patent Application No. 14/111,326, Patent Owner did not “overcome” an *obviousness* rejection over Rissin; the Examiner’s focus was on patent *eligibility*, and cited Rissin as one of many references “in a non-exhaustive list” that “illustrates that at the time of or before the instant invention, an assay meeting the criteria of the instantly claimed assay was already publicly known and had been disclosed as measuring numerous different proteins from cancer antigens to AB to tau.” *Id.* at 6-7 (identifying a non-exhaustive list of fourteen other known “assay[s] meeting the criteria of the instantly claimed assay”). That Patent Owner later overcame the Examiner’s patent eligibility rejection as to certain claims having limitations not present in the Challenged Claims is of no moment to the Petitioner’s obviousness grounds, which were never considered by the Examiner.

**(c) Patent Owner Failed to Notify the
Examiner of the Most Pertinent Art And
of Blatant Examiner Errors**

The Examiner did not cite Rissin during prosecution of the application that issued as the '092 Patent. That was an Examiner's material error that warrants institution. Far worse, however, neither did Patent Owner bring Rissin to the Examiner's attention – despite Patent Owner's intimate knowledge of both the reference and the fact that Rissin disclosed the very limitations Patent Owner argued were not disclosed in the references the Examiner *was* considering. *See* PO DD Brief, Paper No. 9 at 10-12. In addition, in the Reasons for Allowance the Examiner stated, “Ding table 1 lists Applicant's claimed assay (tau Simoa) used by at least forty-two (42) groups”, whereas the assay recitation of claim 1, step (C), by its language is ***not*** expressly limited to a SiMoA assay, and Ding does ***not*** show 42 groups having adopted SiMoA assays for detecting tau – blatant Examiner errors at the core of the claim allowance that Patent Owner never corrected.⁵ EX-1002, 659. These are material errors that simply cannot stand.⁶

⁵ A further Examiner error warranting institution of IPR proceedings is the withdrawal of the § 103 rejection in the absence of evidence.

⁶ Information is “material” under 37 C.F.R. § 1.56(b) if it establishes unpatentability of a claim, or refutes or is inconsistent with a position an applicant

The Examiner relied on two primary references during prosecution: Duffy in view of Quanterix 2010a (i.e., two references disclosing the use of ultra-sensitive SiMoA assays to detect low-level biomarker in the blood of patients that were owned by Patent Owner itself). In response, Patent Owner sought to overcome the Examiner's rejection on grounds that the SiMoA assay taught by Duffy "differed" from the claimed invention in two material ways.

First, Patent Owner argued that Duffy utilized capture antibodies immobilized at "fixed locations" on the reaction vessel, whereas the claimed method recites a "suspension" of capture objects (i.e., beads) in a diluted bodily fluid. Patent Owner argued that suspending the capture objects "allowed for

takes in opposing an argument of unpatentability relied on by the USPTO or in asserting an argument of patentability. Under *Therasense, Inc. v. Becton, Dickinson & Co.*, 649 F.3d 1276 (Fed. Cir. 2011), information is "but-for" material if but-for an applicant's withholding of information the patent would not have granted. Each of Patent Owner's failure to bring Rissin to the Examiner's attention, failure to cite Quanterix's May 29, 2010 website (EX-1030), and failure to correct the Examiner's errors as to Ding in the Reasons For Allowance were both the withholding of Rule 56 material and *Therasense* but-for material information.

improved analyte-binding efficiency” compared to immobilized antibodies of Duffy. *See* EX-1002, 563-64.

Second, Patent Owner argued that Duffy required an additional step not required by the Challenged Claims. That is, after the analyte molecules were bound to the immobilized antibody, at least a portion of the immobilized complexes were “disassociated” or “released” back into the fluid sample. The analyte concentration was then determined based upon the number of released complexes. Patent Owner argued that such a “release/disassociation step” is not required by the Challenged Claims, which operate by detecting analyte concentration directly from the suspended capture objects. *See* EX-1002, 564.

In response, the Examiner indicated that “if [issued claim 12] was a non-obvious improvement as alleged, then the claim might be sufficient to overcome the 103 rejection” over Duffy in view of Quanterix 2010a. *Id.* at 627.

Yet, at the time of this interview (and in the weeks and months that followed) Patent Owner was well aware that Rissin taught a SiMoA technique utilizing *both* of these alleged “differences”, and that the Examiner had not considered the closest prior art, but nonetheless failed to notify the Examiner of the error. Because the Examiner specifically found these features missing in the cited art, Patent Owner should have identified the relevancy of Rissin, rather than burying that reference in an IDS and saying nothing. *Armour & Co. v. Swift &*

Co., 466 F.2d 767, 779 (7th Cir. 1972) (“[W]e think that it is unfair to [assume] a busy Examiner... retains details of every pending file in his mind when he is reviewing a particular application...[T]he applicant has the burden of presenting the Examiner with a complete and accurate record to support the allowance of letters patent.”) (emphasis added); EX-1002, 110-37 (listing references deemed to be material to patentability in an IDS). Instead, Patent Owner sat silent, leading the Examiner down the path of material error based on an incomplete and inaccurate record with full knowledge of the likely outcome of its silence. Moreover, as discussed herein, the Patent Owner also sat silent and did not correct the Examiner’s errors in the Reasons For Allowance, and advanced arguments that were contradicted by Patent Owner’s May 29, 2010 website (EX-1030). The Patent Owner withheld Rule 56 material and *Therasense* but-for material information. On these unlevel grounds, the Examiner materially erred, and the Examiner’s material errors cannot stand.

**(d) Todd Supplies the “Missing” Motivation
Argued by Patent Owner to Obtain
Allowance**

Patent Owner’s arguments that Todd is somehow “cumulative” of the art considered by the Examiner are belied by its own admission that Todd supplies the allegedly “missing” motivation to use ultra-sensitive assays to measure tau levels in blood as a clinical marker for neurological disorders.

On the one hand, Patent Owner argues that Todd (and Voorheis) are “cumulative” of other art because they “offer the same information that Quanterix 2010a, Mortberg and Wunderlich provided during prosecution of the '092 Patent”, including the “motivation to detect tau protein in blood... *with conventional assay techniques.*” PO DD Brief, Paper No. 9 at 20-21 (emphasis added). Patent Owner further argues “at the time of the invention, there was no clear impetus in the field to use ultra-sensitive assay methods to detect tau”, Patent Owner argues, because those “conventional assay methods had been used and generally accepted.” *Id.* at 6-7. Then Patent Owner admits that, “[a]fter considering [these] arguments, the Examiner allowed the claims.” *Id.*

On the other hand, however, Patent Owner admits that Todd *supplies* that missing “*impetus*” to use ultra-sensitive assays to measure tau levels in blood as a clinical marker for neurological disorders (*e.g.*, Alzheimer’s). Indeed, Patent Owner describes, in clear and unambiguous terms, the “biomarker movement” discussed in Todd that was built upon by the recognized need for earlier disease detection and diagnosis of disease states. Patent Owner concedes that:

Todd describes a ‘*biomarker movement*’ in drug discovery and disease diagnosis, and the need to develop advanced protein detection systems. (EX. 1006 at 1-2; Petition, Paper No. 2 at 32.) Among other applications, Todd asserts that protein biomarker programs in

Alzheimer's disease might ***benefit from immunoassay technologies with ultra-sensitive detection***, and identifies 'beta-amyloid and ***tau proteins***' as ***potentially 'hopeful candidates'*** as clinical markers for Alzheimer's diagnosis. (Ex. 1006 at 3; Petition, Paper No. 2 at 33-34.) Todd further reports on "next generation immunoassay systems," including "Single Molecule counting (SMC)-based systems" by Singulex that are capable of 'quantifying biomarkers at the sub-picogram level.' (Ex. 1006 at 3; Petition, Paper No. 2 at 31).

Id. at 19-20.

Thus, Patent Owner admits that Todd bridges the alleged "gap" between the use of "conventional" and "ultra-sensitive" assays to detect tau, undermining not only Patent Owner's argument that Todd is "cumulative", but also the very basis for the Patent Owner's patentability arguments to the Examiner. Simply put, Todd is not cumulative of the art before the Examiner, and the Examiner's failure to uncover Todd, and consider the combination of Rissin in view of Todd, were material errors.⁷

⁷ Todd indeed shows a clear impetus in the field to use ultra-sensitive assays to detect tau, contrary to the Patent Owner's assertions. The Director and the PTAB are also respectfully requested to consider that the state of the art included the

**(e) Patent Owner's Faulty "Sea Change"
Arguments Caused the Examiner to
Materially Error**

Patent Owner also argued that secondary considerations, including an alleged "sea-change in the field" supported patentability and "effectively created or contributed to creating the reasonable expectation of success that was absent at the time Applicant's invention was made...." EX-1002, 555. Patent Owner argued that Tables 1 and 2 in Ding – a review article published almost ten years after the publication of the application – reported results from various research groups using SiMoA to measure blood tau wherein the "vast majority of the reports" came "after the publication of the invention." *Id.* at 560. In response, the Examiner improvidently agreed, concluding that:

Quanterix Presentation (EX-1033) that directed using SiMoA to detect tau, the Patent Owner's May 29, 2010 website (EX-1030) that directed using SiMoA to detect biomarkers of Alzheimer's Disease in blood (tau was understood as a biomarker of Alzheimer's Disease), and the Singulex website (EX-1036) that directed using the ultra-sensitive Erenna system for detecting an Alzheimer's Disease biomarker in blood – with it noted that none of Todd, the Patent Owner's website, nor Singulex's website were before the Examiner in original prosecution.

Of particular relevance, Ding table 1 lists Applicant's claimed assay (tau Simoa) used by at least forty-two (42) groups after the effective filing date of 4/12/11. This is in contrast to the obviousness conclusion set forth by the Examiner, which articulated why it would have been obvious to use Simoa to detect tau, but also recognized that no group had actually done so.... It is on this fact that the Examiner finds the argument persuasive and concludes that the rebuttal evidence is sufficient to overcome the obviousness rejection.

EX-1002, 659-60 (emphasis in original).

Here, not only is Ground 1 based on different art than that which was before the Examiner, but as set forth in the Petition, the Examiner's consideration of Patent Owner's alleged secondary considerations was a material in error because Patent Owner failed to provide any actual evidence, and failed to establish any nexus between the Challenged Claims and the results in Ding.⁸ While Patent

⁸ There is no serious dispute that the '092 Patent file history only contains mere attorney argument as to Patent Owner's supposed secondary considerations. *See* MPEP 2145 I ("Attorney argument is not evidence"; "arguments of counsel cannot take the place of evidence"); MPEP 716.01(c) II ("arguments of counsel cannot take the place of evidence in the record" (citing *In re Schulze*, 346 F.2d 600, 602

Owner attempts to make light of myriad issues Petitioner raised concerning the Examiner's reliance on Ding – at times deriding Petitioner's valid critiques as “halfhearted” and “quibbles” – Patent Owner provides no substantive response to rebut these issues.

Indeed, as set forth in the Petition, Patent Owner failed to link the alleged increase in the number of groups using SiMoA to quantify blood tau levels to what is both claimed and allegedly novel in the Challenged Claims, as opposed to other factors, including the prior art SiMoA techniques disclosed in Duffy (which is within step (C) of claim 1), or Rissin (which also is within step (C) of claim 1 and teaches the same SiMoA technique as claim 12), or the numerous other SiMoA publications that Patent Owner openly admits were known.

As an initial matter, the Challenged Claims are not limited to SiMoA assays; rather the Challenged Claims encompass any assay capable of meeting the claimed LoD and LoQ parameters recited in the claims (*see* EX-1001, claim 1, “wherein” clause). Thus, Patent Owner's reliance on Ding is a red herring, and speaks

(C.C.P.A. 1965)). “Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding ... commercial success, solution of a long-felt need, [and] inoperability of the prior art”. *Id.*

nothing of the myriad of other ultra-sensitive assays – that Patent Owner *concedes* were well-known – capable of detecting blood biomarkers at the levels recited in the Challenged Claims. *See, e.g.*, EX-1001, claim 1, step (C) (reciting “quantifying through the use of an analytical protein concentration measurement assay” and not “quantifying through the use of an analytical protein concentration measurement SiMoA assay”). This disconnect between the broad scope of the Challenged Claims, and the limited SiMoA assays reviewed in Ding, demonstrates the lack of nexus between the '092 Patent claims and Patent Owner's purported secondary considerations of nonobviousness, and shows that institution of IPR proceedings is warranted.

Rather, Patent Owner's only purported basis supporting the alleged “nexus” was the loose association between the timing of the publications cited in Ding (beginning in 2014) and the publication of an earlier-filed PCT patent application in the priority chain of the '092 Patent (two years earlier). EX-1002, 560 (alleging “the vast majority of reports in Tables 1 and 2 of Ding... came after the publication of International Publication WO2012/142301 on October 18, 2012... which the present application claims priority.”). However, coincidental timing alone does not establish the requisite “nexus” and additional evidence tying the assays of the publications cited in Ding to the underlying claims is needed. *See, e.g., Ancora Techs, Inc. v. Roku, Inc.*, 140 F.4th 1351, 1361 (Fed. Cir. 2025) (holding press

release praising challenged patent generally, versus tying products to patent claims, insufficient to establish nexus).

This is particularly true given that Patent Owner was *commercially marketing* a fully automated SiMoA platform for the detection of pTau in blood in (while pronouncing its alleged “dominating patent position” to the field) *one-year before* the alleged “uptick” in tau-Simoa publications reported in Ding. *See e.g.*, EX-1039 (Patent Owner’s July 30, 2013 Announcement of the “Commercial Availability of its SiMoA Single Molecule Array Technology”); EX-1034 (Patent Owner’s Oct. 22, 2013 webpage showing commercial availability of its SiMoA test kit for tau). And well before the ’092 Patent’s earliest filing date, Patent Owner’s website explicitly taught diagnosing Alzheimer’s Disease using Quanterix’s SiMoA technology. *See* Patent Owner’s May 29, 2010 Website (EX-1030).

Indeed, Ding expressly acknowledged the commercial availability of Quanterix’s pTau detection kit and, in fact, used that commercial availability as a basis for “excluding” publications performed on other assay platforms due to the “challenge” of combining those results “with those using the *commercialized* plasma tau detection kit developed by Quanterix.” EX-1019, 11 (emphasis added). Thus, it is far more likely that the alleged “increase” in the number of SiMoA-based experiments measuring blood tau was the result of the now large-scale commercial availability of a SiMoA pTau assay, than the mere “publication” of a

PCT patent application without more. At minimum, this more plausible explanation warrants a trial on the merits. And neither in these proceedings nor in the original prosecution has Patent Owner pointed to *any* of the Ding forty-two (42) SiMoA publications as citing the PCT patent application as a basis for the use of a SiMoA assay (as opposed to other assays) for the detection of tau in blood; Patent Owner's silence on this point speaks volumes to the fact that the publication of the PCT patent application had absolutely no bearing on the use of SiMoA in any of those forty-two (42) publications cited in Ding.

Moreover, Petitioner's correction that Ding describes forty-two (42) *publications* – not *groups* – using “Applicant's claimed assay (tau Simoa)... after the effective filing date of 4/12/11”, is not simply “quibbling.” It demonstrates that, apart from not recognizing the commercial availability of Patent Owner's tau SiMoA assay, the Examiner also misunderstood both the relevance and scope of studies conveyed in Ding (as well as the express language of the '092 Patent claims that do not expressly recite that the assay is a SiMoA assay). Given that at least 17 of these 42 studies (nearly 50%) were made by authors directly affiliated with Patent Owner, and a large number of the remaining studies were made through affiliations of other authors, the actual number of “groups” of scientists allegedly “adopting” Patent Owner's technology was far fewer than the Examiner was made to understand. Nonetheless, here again Patent Owner failed to notify the

Examiner of the Examiner's errors in allowance (including as to both as to the substance of Ding, and as to the language of the claims being allowed).

In any event, the obviousness arguments set forth in the Petition are so strong that Patent Owner's assertions of secondary considerations, even if presented by way of declaration or affidavit, cannot overcome the final conclusion of obviousness. *See* MPEP 2145 (citing *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007); *Leapfrog Enters Inc. v. Fisher-Price Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007); *Newell Cos., Inc. v. Kenny Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988)).

ii. The Examiner's Error Is Further Evident By Ground 2.

Ground 2. By not considering the combination of Rissin in view of Voorheis, the Examiner also materially erred under the second part of the *Advanced Bionics* test. *Becton* factors (c), (e), and (f) inform this analysis. *Advanced Bionics* at 9-10.

As discussed above, Voorheis was only before the Examiner by virtue of its inclusion in an IDS, and was not used as the basis for any rejection or in combination with Rissin. There was no analysis or discussion of Voorheis' teachings in the prosecution history, and *Becton*, *Dickinson* factor (c) thus weighs against the exercise of discretion under § 325(d). *See Ascend Elements, Inc. v. Duesenfeld GmbH*, IPR2024-00948, Paper 10 at 37 (P.T.A.B. Nov. 22, 2024) (finding that

petitioner has demonstrated that the Office had materially erred where “the Office did not rely on any of the references asserted [] to reject any of the claims challenged here[,]” “so it appears [the asserted obviousness arguments] were overlooked”); *Aylo Freesites Ltd. v. Dish Techs. L.L.C.*, IPR2024-00940, Paper 12 at 33-34 (P.T.A.B. Nov. 21, 2024) (“Neither the applicants nor the Examiner discussed these references and petitions, and the Examiner did not use any of them as a basis of any rejection. Rather, the Examiner’s only interaction with these items appears to be within the context of receiving and responding to Information Disclosure Statements.”); *CODE200, UAB v. Bright Data Ltd.*, IPR2022-00353, Paper 8 at 10 (P.T.A.B. July 1, 2022) (fact that reference was not the basis of rejection in the prosecution of challenged patent “weighs strongly against exercising our discretion to deny institution under 35 U.S.C. § 325(d)”) (citing *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17–18 (P.T.A.B. Dec. 15, 2017); *Kayak Software Corp. v. Int’l Bus. Machs. Corp.*, CBM2016-00075, Paper No. 16 at 11 (P.T.A.B. Dec. 15, 2016)).

The teachings of Voorheis are also highly material to the validity of the Challenged Claims and directly rebut arguments advanced by Patent Owner to secure issuance of the patent. As set forth in the Petition, Voorheis is directed to methods and kits for diagnosing Alzheimer’s Disease (AD) and other neurological disorders by screening for tau in the blood of a patient. Like Todd, Voorheis also

supplies the allegedly missing “motivation” to induce a POSA to develop more sensitive diagnostic tests to screen for the presence of tau biomarkers in blood. Voorheis discusses the frustration felt by patients, doctors and family members as a result of the lack of reliable methods to diagnose the cognitive ability of patients with early on-set AD, and the express need for more sensitive assays to rapidly diagnose the disease, “particularly in the early stages where even a simple arrest of the progress of the disease would leave the patient with significant intellectual capacity and a reasonable quality of life.” EX-1007, 3:25-28.

Thus, Voorheis directly rebuts Patent Owner’s counterfactual argument that – in a disease that effects more than 6-million Americans (one in six in the United States) and costs hundreds of billions of dollars annually in long-term care – POSA’s were somehow content with low sensitivity testing techniques or otherwise disinterested in applying more sensitive assays (which were admittedly well-known in the art) to detect low concentrations of tau biomarkers in bodily fluids earlier, and with increased accuracy and precision. Patent Owner’s argument does not pass the straight-face test, and the Examiner’s failure to consider the teachings of Voorheis was material error.

Moreover, as further detailed in the Petition, Voorheis (in combination with Rissin) teaches and renders obvious all of the limitations of the Challenged Claims, including the assay limitations argued by Patent Owner and improvidently accepted

by the Examiner as being absent from the prior art of record during the applicant interview (but which the Patent Owner knew to be present in their Rissin reference not before the Examiner). *See supra* Section 2(i)(a)-(c); EX-1002, 563-64.

The Petition shows how Voorheis in combination with Rissin does not suffer from the purported deficiencies that Patent Owner argued were present in the art used by the Examiner for rejecting the claims under § 103.

Under *Becton, Dickinson* factor (e), the teachings from Voorheis identified above (and analyzed in greater detail in the identified patentability contentions from the Petition) demonstrate that the Examiner materially erred in the evaluation of the prior art.

The Examiner overlooked (or misapprehended) the teachings from Voorheis (and never considered the identified teachings of Rissin) when mistakenly concluding that issued claim 12 contained certain assay limitations (discussed above) which were “a non-obvious improvement as alleged” by Patent Owner not found in the prior art. EX-1002, 627; *Aylo Freesites*, IPR2024-00940, Paper 12 at 34 (“It is difficult to characterize error in a nearly silent record, and we find that Petitioner has sufficiently demonstrated error based in part on its unpatentability contentions.”).

Finally, the Petition includes additional evidence and facts that were not before the Examiner during prosecution, including, *e.g.*: (i) the prior art references

that are combined with Voorheis in the asserted obviousness grounds (*i.e.*, Rissin and Todd) and (ii) the expert declaration of Dr. John Todd explaining the teachings of Voorheis, Rissin and Todd (which was not before the Examiner) and why a person of ordinary skill would have been motivated and found it obvious to combine them. *See* EX-1003, 43-47, 69-72. *Becton, Dickinson* factor (f) thus further shows material error and weighs against the exercise of discretion under 325(d). *See, e.g., Ascend Elements*, IPR2024-00948, Paper 10 at 37 (Petitioner offered additional evidence including additional references in the asserted obviousness combinations, as well as expert declaration, “that was not before the Office during examination”); *Taro Pharms. U.S.A., Inc.*, IPR2017-01446, Paper 7 at 18 (declining to exercise discretion to deny Petition based on new expert declaration evidence that was not previously presented to the Office).

For these reasons, the Director should decline to exercise her discretion to deny institution under § 325(d).

B. Discretionary Denial Under 35 U.S.C. § 314(a) Is Not Appropriate

i. No Grounds for a *Sotera* Stipulation Were Present When the Petition Was Filed

In what appears to be a last-minute add-on, Patent Owner includes a single-paragraph argument that discretionary denial is appropriate because Petitioner “did not offer a [*Sotera*] stipulation”. Patent Owner’s brevity, however, speaks too much. As Patent Owner must concede, at the time of filing the Petition, the only issue

before the district court was Petitioner's declaratory judgment of *noninfringement* – an issue clearly not before the Board. Patent Owner did not file its infringement counterclaim – giving rise to a potential invalidity challenge before the district court – until several months later. Stated different, there was no basis upon which to file a *Sotera* stipulation with the Petition.

That same posture remains even today. To date, Petitioner has not raised any validity challenges before the District Court that could be (or could have been) raised before the Board in the Petition. Rather, the only invalidity challenge raised so far – indeed the only substantive activity in the case at all – is a challenge for lack of patent eligibility under 35 U.S.C. §101 raised by Fujirebio Diagnostics, Inc. (FDI, Petitioner herein) by way of a motion to dismiss under Fed. R. Civ. P. 12(b)(6) for failure to state a claim. Like non-infringement, the question of patent eligibility is one that clearly falls outside the jurisdiction of the Board and, thus, there is no overlap in issues between the Petition and the district court litigation (*see* fn 4, *supra*).

Nonetheless, in order to avoid any potential overlap between the two proceedings, Petitioner provides herewith a *Sotera* stipulation certifying that, if IPR proceedings are instituted, neither Petitioner (FDI) nor counter-claim defendant Fujirebio Europe N.V. (FRE) will pursue in the district court litigation (1) the specific invalidity grounds that Petitioner raised in the IPR petition, nor (2) any other

invalidity ground that Petitioner could have reasonably raised in the IPR petition under §§ 102 or 103, against the asserted claims of the patent-in-suit, nor (3) any invalidity ground based on a combination of system prior art and the references asserted in the Petition.

Patent Owner's arguments under 35 U.S.C. § 314(a) are, therefore, moot.

ii. The *Fintiv* Factors Support Institution

The remaining *Fintiv* factors nonetheless caution against discretionary denial. In determining whether to exercise discretion under 35 U.S.C. § 314(a) to deny institution in view of a parallel proceeding, the Board developed a framework that includes consideration of six factors (the “*Fintiv* factors”). *See Apple Inc. v. Fintiv, Inc.*, No. IPR2020-00019, Paper 11 at 5-6 (P.T.A.B. Mar. 20, 2020).

“These factors relate to whether efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in the parallel proceeding.” *Id.* 6. In evaluating the *Fintiv* factors, the Board takes “a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review,” recognizing that “there is some overlap among these factors” and that “[s]ome facts may be relevant to more than one factor.” *Id.* More recently, on March 26, 2025, the Director issued a memorandum identifying additional exemplary discretionary criteria that may be considered and stating that

parties are “permitted to address all relevant considerations.” Memorandum: Interim Processes for PTAB Workload Management, March 26, 2025 at 2.⁹

While Patent Owner failed to engage any analysis of the established discretionary denial factors, as briefly set forth below, the sum of factors weighs against discretionary denial here. The *Fintiv* factors are all either neutral or weigh against discretionary denial:

- **Factor 1: whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted** – neither party to the district court proceeding has requested a stay, and the question of non-infringement before the district court differs significantly from the validity issues before the Board. The only invalidity challenge raised before the district court so far is a challenge for lack of patent eligibility under 35 U.S.C. §101 raised by Petitioner by way of a motion to dismiss under Fed. R. Civ. P. 12(b)(6) for failure to state a claim. If the Board institutes IPR, and the district court litigation is not dismissed by way of the currently pending motion to dismiss, Petitioner intends to seek a stay of the district court litigation pending resolution of this IPR. This factor is neutral.

⁹ Available at <https://www.uspto.gov/sites/default/files/documents/>

- **Factor 2: proximity of the court's trial date to the Board's projected statutory deadline for a final written decision** – In the district court litigation, issue has not been joined, no scheduling order has been entered, and there is no trial date set. Moreover, given the current procedural posture of that case, briefing and argument on counterclaim defendants Fed. R. Civ. P. 12(b)(6) motions to dismiss will not likely be completed before the end of the year, and a decision on those motions is not expected for many months thereafter. According to the latest statistics, the median time from filing to trial in the District of Delaware is 35 months and thus, even absent a stay, any trial would take place 18 months after the expected December 2026 date for a final written decision, thus supporting institution of IPR.¹⁰

- **Factor 3: investment in the parallel proceeding by the court and the parties** – the district court litigation is still in its nascent stages. The Court has not scheduled (much less held) an initial scheduling conference, and there are no fixed deadlines currently set for the close of fact discovery, expert discovery, dispositive motions or trial; showing that almost all of the investment in the parallel litigation still lies ahead. This factor supports institution of IPR.

¹⁰https://www.uscourts.gov/sites/default/files/document/fcms_na_distprofile0630.2025.pdf.

- **Factor 4: overlap between issues raised in the petition and in the parallel proceeding** – the issues currently before the district court relate to non-infringement, lack of specificity in Patent Owner's counterclaims, and patent ineligibility under section 101; those issues will not be before the Board.

Moreover, Petitioner's *Sotera* stipulation eliminates any potential overlap of issues and, thus, supports institution.

- **Factor 5: whether the petitioner and the defendant in the parallel proceeding are the same party**—both Petitioner (Fujirebio Diagnostics Inc.) and Patent Owner (Quanterix) are parties in the district court litigation. Thus, this factor supports granting institution.

- **Factor 6: other circumstances that impact the Director's exercise of discretion, including the merits** – other considerations, including the strength of the Petition, the absence of settled expectations, and the ability to correct a material error made by the Office in improvidently issuing the Challenged Claims (discussed further below), also support institution and weigh against discretionary denial.

A holistic review of the foregoing *Fintiv* factors, namely that the timing of the Petition was reasonable, the relatively limited investment in the parallel proceeding to date, and that there is no potential overlap of the two proceedings,

and the presence of strong, well-supported prior art grounds tilts the *Fintiv* factors in favor of instituting *inter partes* review.

iii. The Director's Additional Discretionary Denial Factors Support Institution

The Director's March 26, 2025 multi-factor discretionary denial test, including the parties' settled expectations, the public's economic interests, the Petition's compelling merits, and efficiency considerations, all weigh against denial.

(a) No Settled Expectations Where Parties Have No Prior Interaction in IPR Context

There are no settled expectations that the '092 Patent would not be subject to IPR challenge. The question of "settled expectations" presupposes a course of dealing or a history of reliance between the parties; it protects parties who have structured their affairs around the status quo. But where two parties do not have a prior relationship—which is explicitly the case here—these reliance interests simply do not exist. There has been no prior licensing, no market dealings, no shared understandings, and no other conduct by which one party relied on the behavior or assertions of the other party regarding the patent. Moreover, the '092 Patent issued on March 15, 2022 (EX-1001), which is only a little over two years before the Petition was filed. Thus, the lack of any settled expectations and this early challenge to the '092 Patent favors institution. *Zhuhai Cosmx Battery Co. v. Ningde Ampere*

Tech. Ltd., IPR2025-00385, Paper 9 at 3 (P.T.A.B. July 2, 2025) (“[T]he early challenges to the patents tip the balance against discretionary denial.”).

**(b) The Public Interest Strongly Favors
Removing Patent Barriers to Alzheimer's
Disease Assays**

Another important consideration to institution, but ignored by Patent Owner, is the question of the public interest. Here, the public interest weighs heavily in favor of the Board's review of dubious patent rights that could prevent life-saving diagnostic assays for Alzheimer's disease from reaching the market.

Courts have long recognized that equitable considerations in patent disputes extend beyond private commercial interests to the impact on public health. *See eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 396–97 (2006) (Kennedy, J., concurring) (emphasizing the importance of considering the public consequences of injunctive relief). When the product at issue is a diagnostic test capable of diagnosing a devastating and progressive disease such as Alzheimer's Disease, the equities and the public interest strongly favor institution on the merits of the Petition.

First, Alzheimer's Disease represents a profound public health crisis. As set forth in the Petition, more than six million Americans are currently living with Alzheimer's Disease, and the number is projected to rise sharply as the population ages. Early and accurate detection is critical to medical management, care

planning, enrollment in clinical trials, and the development of new therapies. On May 16, 2025, Petitioner received FDA clearance under the “Breakthrough Device Designation” to market the first *in vitro* diagnostic device that tests blood to aid in diagnosing Alzheimer’s disease (see FDA 5/16/25 News Release, EX-1046).

Allowing an invalid patent to remain an obstacle on which to deny patients and physicians access to reliable diagnostic assays (or that increases the cost of reliable diagnostic assays) stymies the ability of individuals to make informed medical decisions and forecloses opportunities for early intervention, which is widely acknowledged to improve quality of life and reduce overall healthcare costs.

Second, the patent system exists to promote—not hinder—innovation and the dissemination of beneficial technologies. *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146 (1989) (“[T]he “ultimate goal” of the patent system is to bring “new designs and technologies into the public domain through disclosure.”). The existence of invalid patents – granted on obvious variations of well-known concepts – undermines that purpose and serves only to restrict patient access to a diagnostic that addresses an unmet medical need.

Finally, the ’092 Patent threatens not only individual patient access, but also the advancement of biomedical research. Diagnostic access accelerates the enrollment of patients into clinical trials for new treatments, directly fueling therapeutic innovation. Restricting access to such assays (and/or increasing the

cost of such assays) thus delays both immediate patient benefits and long-term breakthroughs, compounding the harm to public welfare. Thus, when viewed in light of the strength of the arguments set forth in the Petition, the public interest overwhelmingly supports a thorough examination of the validity of the '092 Patent through institution of IPR proceedings.

(c) The Strength of the Petition and Efficient Use of the Board's Resources Warrant Institution

The strength of the Petition warrant institution because the Petition demonstrates, on the face of the record, a strong likelihood that the Challenged Claims are unpatentable. The Board and the Director have made clear that the strength of the petition weighs in favor of institution, regardless of other discretionary considerations. *See Apple Inc.*, IPR2020-00019, Paper 11 at 16 (identifying the strength of the merits as a relevant factor in the discretionary denial analysis).

Likewise, the Supreme Court has also recognized that the IPR framework was designed to improve patent quality and correct improvidently granted claims. *See Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 279 (2016) (IPR serves as a “second look at an earlier administrative grant” of patent rights to improve accuracy and public confidence). Denying institution despite compelling evidence

of unpatentability would disserve this statutory purpose by perpetuating enforcement of invalid claims.

Here, the merits of the Petition are strong, presenting a compelling case of unpatentability: the prior art references map directly onto the limitations of the Challenged Claims, the combinations are supported by explicit teachings and motivation to combine, and expert testimony corroborates the technical rationale with unrebutted evidence.

The Petition presents a straightforward combination of the teachings of Rissin (EX-1005) with Todd (EX-1006) or Voorheis (EX-1007) that render obvious the Challenged Claims. *See* Pet. at 4 (listing asserted grounds). In response, Patent Owner admits that tau was a well-known biomarker for neurological disorders, and further that assays that were capable of detecting ultra-low concentrations of analyte (including its own SiMoA assay –as disclosed in Rissin) were well-known in the art. Todd and Voorheis squarely provide the motivation found missing during prosecution to apply Rissin's well-known ultra-sensitive assay to detect tau levels in the blood of patients suspected of having neurological conditions, and the wide-spread prevalence and societal costs of Alzheimer's disease provided more than enough incentive to do so.

The Petition shows that skilled artisans would have applied Rissin's teachings with those of Todd and/or Voorheis in a way that renders the Challenged

Claims unpatentable. Taken together, these grounds not only meet but exceed the “reasonable likelihood” threshold under 35 U.S.C. § 314(a).

Finally, instituting review would be an efficient and appropriate use of the Board’s resources, particularly to correct the material errors the Office made in improvidently granting the Challenged Claims. Critically, the material error of the Office was caused by the Patent Owner’s misrepresentation of the prior art. It would be manifestly unfair to allow the Patent Owner to benefit again from its misrepresentation by discretionarily denying review. The Petition presents only two clear, well-supported grounds that go directly to the core validity of the Challenged Claims, ensuring that the proceeding will focus on discrete, dispositive issues rather than diffuse or speculative disputes. The PTAB was designed as a streamlined, expert forum for resolving such technical validity questions far more efficiently than district court litigation. *See Cuozzo Speed*, 579 U.S. at 267-68; *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1079 (Fed. Cir. 2015) (“Board members, because of expertise, may more often find it easier to understand and soundly explain the teachings and suggestions of prior art without expert assistance.”). Here, the strong merits and narrow grounds maximize the likelihood that the Board’s investment of resources will yield a clear and conclusive resolution, fulfilling Congress’s intent that IPR provide a cost-effective mechanism to improve patent quality and conserve judicial and agency resources.

Accordingly, the Board should institute *inter partes* review to ensure that the Challenged Claims receive the scrutiny Congress intended, and to prevent the continued assertion of claims that are highly likely to be invalid in light of the prior art.

III. CONCLUSION

For the reasons set forth above, Petitioner has established a reasonable likelihood of prevailing with respect to all Challenged Claims of the '092 Patent and requests the Board institute *inter partes* review and then cancel the Challenged Claims as unpatentable.

Respectfully submitted,

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Dated: September 19, 2025

CERTIFICATION OF SERVICE ON PATENT OWNER

Pursuant to 37 C.F.R. §§ 42.6(e), 42.8(b)(4) and 42.105, the undersigned certifies that on September 19, 2025, a complete and entire copy of Petitioner's Opposition to Patent Owner's Request for Discretionary Denial of Institution and all supporting exhibits were served via email to counsel for Patent Owner at the following addresses of record:

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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24 *et seq.*, the undersigned certifies that this document complies with the type-volume limitations. Excluding the Table of Contents, Table of Authorities, Mandatory Notices, Certificates of Service and Word Count, and Appendix (or List) of Exhibits, this document contains 10,073 (less than 14,000) words as calculated by the “Word Count” feature of Microsoft Word 2010, the word processing program used to create it.

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