UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Padagis US LLC,
Petitioner

v.

Neurelis, Inc.,
Patent Owner

Case No. IPR2025-00465
Patent No. 11,241,414

PATENT OWNER'S SUR-REPLY

TABLE OF CONTENTS

TABLE OF CONTENTS i
TABLE OF AUTHORITIES iii
TABLE OF EXHIBITS vi
I. COLLATERAL ESTOPPEL DOES NOT APPLY 1
A. Issues Materially Differ 1
1. '414 Patent Priority Date 2
2. Obviousness over Gwozdz-PCT and Meezan 3
B. Issues Were Not Actually Litigated 4
1. Non-Obviousness over Gwozdz-PCT and Meezan 4
2. '414 Patent Priority Date 5
3. Priority of Gwozdz-PCT 6
II. PETITIONER CONFLATES §103(c) PROVISIONS 6
III. GWOZDZ-PCT IS NOT PRIOR ART 7
A. The Sigma Catalog Is Incorporated with Particularity 7
B. The Sigma Catalog Can Be Incorporated 8
1. Petitioner Fails to Address *Acqis* 8
2. Petitioner Fails to Address *Neurent* and M.P.E.P. §608.01(p) 8
3. Sigma Catalog Is Not Necessary to Provide Written-Description Support 11
C. The '558 Provisional Provides Sufficient Support 12
1. Blaze Marks Are Not Required 12
2. The '558 Provisional Provides Blaze Marks 13
IV. THE CHALLENGED CLAIMS ARE NOT OBVIOUS 13
A. Failure to Disclose or Suggest All Claim Limitations 14
1. No Disclosure or Suggestion of *n*-dodecyl-β-D-Maltoside 14
a. Petitioner Belatedly Applies IUPAC Naming 15
b. Meezan Teaches the Opposite of the Claimed Compound 17
c. New Evidence Does Not Support Obviousness 18
d. No Motivation Toward *n*-dodecyl-β-D-maltoside 19

2. No Disclosure or Suggestion of Non-Aqueous Solutions 20
a. Petitioner's Improper Claim Construction Tactics.....20
b. Petitioner Shifts to New Theories in Reply 22
c. No Motivation to Combine 22
B. Petitioner's Generic Motivations Do Not Establish Obviousness 24
1. Gwozdz-PCT Solves the Problem of Bioavailability 25
2. Gwozdz-PCT Solves the Problem of Solubility 25
3. The Combination Does Not Improve Stability.....26
C. Petitioner's Reliance on "Other Pharmaceutically Acceptable Additives" and "Wetting Agents".....28
D. Meezan Is Directed To Macromolecules and Does Not Address Compatibility with Tocopherol Solutions.....28
V. CONCLUSION.....29
CERTIFICATION OF WORD COUNT 31
CERTIFICATE OF SERVICE 32

TABLE OF AUTHORITIES

Page(s)

Cases

ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.,
694 F.3d 1312 (Fed. Cir. 2012).....24

Advanced Display Sys., Inc. v. Kent State Univ.,
212 F.3d 1272 (Fed. Cir. 2000).....7

Allergan USA, Inc. v. MSN Lab'ys Priv. Ltd.,
111 F.4th 1358 (Fed. Cir. 2024) 12

Apple Inc. v. Andrea Elecs. Corp.,
949 F.3d 697 (Fed. Cir. 2020).....14

Apple Inc. v. DoDots Licensing Solutions LLC,
IPR2023-00939, Paper 12 (P.T.A.B. Jan. 3, 2024).....18

Ariad Pharms., Inc. v. Eli Lilly & Co.,
598 F.3d 1336 (Fed. Cir. 2010).....12

Ariosa Diagnostics v. Verinata Health, Inc.,
805 F.3d 1359 (Fed. Cir. 2015).....22

Atofina v. Great Lakes Chem. Corp.,
441 F.3d 991 (Fed. Cir. 2006).....3

Belden Inc. v. Berk-Tek LLC,
805 F.3d 1064 (Fed. Cir. 2015).....3

Callaway Golf Co. v. Acushnet Co.,
576 F.3d 1331 (Fed. Cir. 2009).....7

Fujikawa v. Wattanasin,
93 F.3d 1559 (Fed. Cir. 1996).....12

Google v. Hammond Development Int'l, Inc.,
54 F.4th 1377 (Fed. Cir. 2022) 4, 6

Harmonic Inc. v. Avid Tech., Inc.,
815 F.3d 1356 (Fed. Cir. 2016).....14

Henny Penny Corp. v. Frymaster LLC,
938 F.3d 1324 (Fed. Cir. 2019)..... 16, 28

In re Fine,
837 F.2d 1071 (Fed. Cir. 1998).....23

In re Fulton,
391 F.3d 1195 (Fed. Cir. 2004).....19

In re Riggs,
131 F.4th 1377 (Fed. Cir. 2025) 6

Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.,
821 F.3d 1359 (Fed. Cir. 2016).....19

KSR Int'l Co. v. Teleflex Inc.,
550 U.S. 398 (2007).....27

MaxLinear, Inc. v. CF CRESPE LLC,
880 F.3d 1373 (Fed. Cir. 2018).....1

Medtronic, Inc. v. Teleflex Innovations S.a.r.l.,
69 F.4th 1341 (Fed. Cir. 2023) 26

Mentor Graphics Corp. v. EVE-USA, Inc.,
851 F.3d 1275 (Fed. Cir. 2017).....11

Neurent Med. Inc. v. The Foundry, LLC,
IPR2024-00669, Paper 8 (P.T.A.B. July 23, 2024) 10, 11

Novartis Pharm Co., v. Shilpa Pharma, Inc.,
IPR2022-00886, Paper 75 (P.T.A.B. Sep. 29, 2023).....7

Ohio Willow Wood Co. v. Alps South, LLC,
735 F.3d 1333 (Fed. Cir. 2013).....2

Paice LLC v. Ford Motor Co.,
881 F.3d 894 (Fed. Cir. 2018).....7

PAR Pharm., Inc. v. TWI Pharms., Inc.,
773 F.3d 1186 (Fed. Cir. 2014).....3

ParkerVision, Inc. v. Qualcomm Inc.,
116 F.4th 1345 (Fed. Cir. 2024) 1

Pers. Web Techs., LLC v. Apple, Inc.,
848 F.3d 987 (Fed. Cir. 2017).....25

Purdue Pharma L.P. v. Depomed, Inc.,
643 F. App'x 960 (Fed. Cir. 2010).....26

Purdue Pharma L.P. v. Faulding Inc.,
230 F.3d 1320 (Fed. Cir. 2000).....12

Purdue Pharma L.P. v. Iancu,
767 F. App'x 918 (Fed. Cir. 2019).....4

Regents of the Univ. of Minn. v. Gilead Sciences, Inc.,
61 F.4th 1350 (Fed. Cir. 2023) 13

Revvo Techs., Inc. v. Cerebrum Sensor Techs., Inc.,
IPR2025-00632, Paper 20 (P.T.A.B. Nov. 3, 2025) (precedential)..... 21, 22

Samsung Electrons. Co. v. Acqis LLC,
IPR2021-00608, Paper 10 (P.T.A.B. Dec. 8, 2021) 8

Soverain Software LLC v. Victoria's Secret Direct Brand Mtmt., LLC,
778 F.3d 1311 (Fed. Cir. 2015).....2

Tesla, Inc. v. Intellectual Ventures II LLC,
IPR2025-00340, Paper 18 (P.T.A.B. Nov. 5, 2025) (informative).....21

TQ Delta, LLC v. 2Wire, Inc.,
No. 13-1835-RGA, 2021 WL 2671296 (D. Del. June 29, 2021) 4

Virtek Vision Int'l ULC v. Assembly Guidance Sys., Inc.,
97 F.4th 882 (Fed. Cir. 2024) 27

Statutes

35 U.S.C. §103(c) (pre-AIA) 8

35 U.S.C. §111(b) 8

Other Authorities

M.P.E.P. §608.01(p)..... 9, 11, 12

Regulations

37 C.F.R. §1.57(c).....7

37 C.F.R. §1.57(d) 8

37 C.F.R. §1.57(g) 11

37 C.F.R. §42.104(b)(2).....18

37 C.F.R. §42.104(b)(3).....21

TABLE OF EXHIBITS

Exhibit	Description of Exhibits
2001	*Clinical Superiority Findings*, U.S. FOOD & DRUG ADMIN. (Dec. 18, 2024) https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/clinical-superiority-findings
2002	Scheduling Order entered in *Neurelis, Inc. v. Padagis LLC*, 1:24-cv-00562, D.I. 20 (D. Del. Aug. 28, 2024)
2003	Preliminary Invalidity Contentions served in *Neurelis, Inc. v. Padagis LLC*, 1:24-cv-00562 (D. Del. Dec. 20, 2024)
2004	Markman Order entered in *Gilead Sciences, Inc. v. Lupin Ltd.*, 1:22-cv-00615-MN, D.I. 280 (D. Del. Feb. 21, 2025)
2005	Markman Order entered in *Spinal Generations, LLC v. Depuy Synthes, Inc.*, 1:22-cv-01368 (MN), D.I. 147 (D. Del. Oct. 16, 2024)
2006	Orange Book Listing for U.S. Patent No. 11,241,414
2007	Declaration of Nicholas A. Peppas, Sc.D., dated December 6, 2018 in *Aquestive Therapeutics, Inc. v. Hale Biopharma Ventures, LLC*, IPR2019-00451, Exhibit 1041 (Jan. 29, 2019)
2008	Declaration of Daniel P. Wermeling, Pharm.D., dated January 27, 2020 in *Aquestive Therapeutics, Inc. v. Hale Biopharma Ventures, LLC*, IPR2019-00451, Exhibit 1150 (Jan. 28, 2020)
2009	Application No. 18/782,666 ("'666 Application")
2010	Information Disclosure Statements filed with the Application No. 18/782,666 ("'666 Application") Prosecution History
2011	Sai H. S. Boddu, Sneha Kumar, A Short Review on the Intranasal Delivery of Diazepam for Treating Acute Repetitive Seizures. Pharmaceutics 2020; 12, 1167

Exhibit	Description of Exhibits
2012	Cornett et al., VALTOCO® (Diazepam Nasal Spray) for the Acute Treatment of Intermittent Stereotypic Episodes of Frequent Seizure Activity, Neurology International 2021; 13:64–78
2013	Scheduling Oral Order entered in *Neurelis, Inc. v. Padagis LLC*, 1:24-cv-00562, D.I. 47 (D. Del. March 11, 2025) Order Granting Stipulation to Extend Certain Fact Discovery Deadlines entered in *Neurelis, Inc. v. Padagis LLC*, 1:24-cv-00562, D.I. 65 (D. Del. May 15, 2025)
2014	Jacqueline A. French, Timothy A. Pedley, *Initial Management of Epilepsy*, New England Journal of Medicine 2008; 359:166-76 ("French & Pedley 2008")
2015	Penovich et al., *Burden of Seizure Clusters on Patients With Epilepsy and Caregivers*, The Neurologist 2017; 22: 207-214
2016	Cloyd et al., *Overcoming the Challenges of Developing an Intranasal Diazepam Rescue Therapy for the Treatment of Seizure Clusters*, Epilepsia 2021; 62:846-856
2017	Hogan, R.E., et al., *Bioavailability and Safety of Diazepam Intranasal Solution Compared to Oral and Rectal Diazepam in Healthy Volunteers*, Epilepsia, 61:455-464 (Feb. 2020)
2018	Lindsay M. Higdon and Michael R. Sperling, *A Review of a Diazepam Nasal Spray for the Treatment Of Acute Seizure Clusters and Prolonged Seizures*, J Expert Review of Neurotherapeutics 2021; 21(11):1207-1212
2019	Bechgaard et al., *Solubilization of Various Benzodiazepines for Intranasal Administration, a Pilot Study*, Pharmaceutical Development and Technology 1997; 2(3):293-296
2020	Gizurarson, S., et al., *Intranasal Administration of Diazepam Aiming at the Treatment of Acute Seizures: Clinical Trials in Healthy Volunteers*, Biol. Pharm. Bull., 22(4):425-427 (Apr. 1999)

Exhibit	Description of Exhibits
2021	Ivaturi, V.D., et al., *Bioavailability and Tolerability of Intranasal Diazepam in Healthy Adult Volunteers*, Epilepsy Res., 84:120-126 (2009)
2022	Schrier, L., et al., *Pharmacokinetics and Pharmacodynamics of a New Highly Concentrated Intranasal Midazolam Formulation for Conscious Sedation*, Brit. J. Clin. Pharmacol., 83:721-731 (Apr. 2017)
2023	Penovich et al., *Benzodiazepines for the Treatment of Seizure Clusters*, CNS Drugs 2024; 38:125-140
2024	Kapoor et al., *A Review of Intranasal Formulations for the Treatment of Seizure Emergencies*, Journal of Controlled Release 2016; 237: 147-159
2025	Rabinowicz et al., *Improvement of Intranasal Drug Delivery with Intravail® Alkylsaccharide Excipient as a Mucosal Absorption Enhancer Aiding in the Treatment of Conditions of the Central Nervous System*, Drugs in R&D 2021; 21:361-369
2026	Acorda Therapeutics, Letter to Plumiaz Clinical Trial Participants, May 20, 2016
2027	U.S. Patent No. 6,193,985 ("Sonne")
2028	Corrected Opening Brief for Appellee Aquestive Therapeutics, Inc. in *Neurelis, Inc. v. Aquestive Therapeutics, Inc.* (Fed. Cir. 21-1038), dated March 31, 2021 (D.I. 21)
2029	Certified transcription of October 5, 2021 oral hearing in *Neurelis, Inc. v. Aquestive Therapeutics, Inc.* (Fed. Cir. 21-1038)
2030	Written joint research agreement, titled "Master Service Agreement" (7 pages), between Particle Sciences, Inc. and Questcor Pharmaceuticals, Inc., dated April 1, 2007 **[FILED UNDER SEAL]**

Exhibit	Description of Exhibits
2031	Asset Purchase Agreement between Hale BioPharma Ventures, LLC and Questcor Pharmaceuticals, Inc., dated June 27, 2008 **[FILED UNDER SEAL]**
2032	H.R. Rep. No. 108-425 (2004)
2033	150 Cong. Rec. S7520-05 (2004)
2034	Non-disclosure Agreement between Aegis Therapeutics, LLC and Questcor Pharmaceuticals, Inc., dated August 15, 2005 **[FILED UNDER SEAL]**
2035	Confidentiality Agreement between Particle Sciences, Inc. and Questcor Pharmaceuticals, Inc., dated January 19, 2007 **[FILED UNDER SEAL]**
2036	Email between Questcor Pharmaceuticals, Inc. and Aegis Therapeutics, LLC, dated February 15, 2007 **[FILED UNDER SEAL]**
2037	Quote No. QCR 135 between Particle Sciences, Inc. and Questcor Pharmaceuticals, Inc., dated March 28, 2007 **[FILED UNDER SEAL]**
2038	QSC-002 Project Email Thread between Aegis Therapeutics, LLC and Questcor Pharmaceuticals, Inc., dated March 26, 2007
2039	Redline Comparison between U.S. Patent No. 11,793,786 and U.S. Patent No. 11,241,414
2040	QC and PSI Agreement between Particle Sciences, Inc. and Questcor Pharmaceuticals, Inc., dated April 2, 2008 **[FILED UNDER SEAL]**
2041	Letter Agreement, with Term Sheet between Neurelis, Inc. and Aegis Therapeutics, LLC, dated August 28, 2007 **[FILED UNDER SEAL]**

Exhibit	Description of Exhibits
2042	Supply Agreement Neurelis, Inc. and Aegis Therapeutics, LLC, dated May 22, 2008 **[FILED UNDER SEAL]**
2043	License Agreement Neurelis, Inc. and Aegis Therapeutics, LLC, dated May 22, 2008 **[FILED UNDER SEAL]**
2044	Transmittal Notice of Intravail from Aegis Therapeutics, dated October 2, 2008 **[FILED UNDER SEAL]**
2045	Declaration of Steven Cartt **[FILED UNDER SEAL]**
2046	Declaration of Dr. Mark Mitchnick **[FILED UNDER SEAL]**
2047	Declaration of David Hale
2048	Redline Comparison between U.S. Patent Application No. 15/955,397 and U.S. Patent Application No. 17/228,514
2049	Marc Brown *Curriculum Vitae*
2050	Joint Claim Construction Brief, *Neurelis, Inc. v. Padagis LLC et al.*, 1:24-cv-00562, D.I. 87 (D. Del. August 15, 2025) ("Joint CC Brief")
2051	Andrew Streitwieser, INTRODUCTION TO ORGANIC CHEMISTRY (4th ed. 1992) ("Streitwieser")
2052	David W. Oxtoby et al., PRINCIPLES OF MODERN CHEMISTRY (4th ed. 1999) ("Oxtoby")
2053	European Pharmacopoeia 6.0, Vol 2 (6th ed. 2007) ("PhEur 6.0")
2054	Panayiotis P. Constantinides et al., *Advances in the Use of Tocols as Drug Delivery Vehicles*, 23 PHARM RES. 243 (2006) ("Constantinides-2006")
2055	Rowe, Sheskey, & Owen, HANDBOOK OF PHARMACEUTICAL EXCIPIENTS, (6th ed. 2009) ("Rowe-2009")

Exhibit	Description of Exhibits
2056	Afaf Kamal-Eldin, *Effect of Fatty Acids and Tocopherols on the Oxidative Stability of Vegetable Oils*, 108 EUR. J. OF LIPID SCI. & TECH. 1051 (2006) ("Kamal-Eldin-2006")
2057	Branka Rozman & Mirjana Gašperlin, *Stability of Vitamins C and E in Topical Microemulsions for Combined Antioxidant Therapy*, 14 DRUG DELIVERY 235 (2008) ("Rozman-2007")
2058	Afaf Kamai-Eldin & Lars-Ake Appelqvist, *The Chemistry and Antioxidant Properties of Tocopherols and Tocotrienols*, 31 LIPIDS 671 (1996) ("Kamai-Eldin-1996")
2059	March 2009 FDA Inactive Ingredient Database
2060	Redline Comparison between U.S. Patent Application No. 12/413/439 and U.S. Patent Application No. 15/955,397
2061	David Ward, *Optimizing Nasal Products for Systemic Delivery*, 106 ONDRUGDELIVERY 56 (2020) ("Ward-2020")
2062	C. Holvoet et al., *Inclusion Complexation of Diazepam with Different Cyclodextrins in Formulations for Parenteral Use*, 60 PHARMAZIE 598 (2005) ("Holvoet-2005")
2063	Sila-On et al., *Influence of Incorporation Methods on Partitioning Behavior of Lipophilic Drugs into Various Phases of a Parenteral Lipid Emulsion*, 9 PHARMSCITECH 684 (2008) ("Sila-On-2008")
2064	D. J. Van Drooge et al., *Incorporation of Lipophilic Drugs in Sugar Glasses by Lyophilization using a Mixture of Water and Tertiary Butyl Alcohol as Solvent*, 93 J. OF PHARM. SCI. 713 (2004) ("Van Drooge-2004")
2065	L. M. A. Monzon & L. M. Yudi, *Voltammetric Analysis of Lipophilicity of Benzodiazepine Derivatives at the Water 1,2-dichloroethan Interface*, 495 J. OF ELECTROANALYTICAL CHEM. 146 (2001) ("Monzon-2001")

Exhibit	Description of Exhibits
2066	M. Molero-Monfort et al., *Retention-activity Relationship Studies of Benzodiazepines by Micellar Liquid Chromatography*, 13 BIOMED. CHROMATOGRAPHY 394 (1999) ("Molero-Monfort-1999")
2067	M. Molero-Monfort et al., *Micellar Liquid Chromatography for Prediction of Drug Transport*, 870 J. OF CHROMATOGRAPHY 1 (2000) ("Molero-Monfort-2000")
2068	Neurelis Patent Family Tree
2069	Declaration of Mareen Donovan, Ph.D. in Support of Defendants' Responsive Claim Construction Brief, *Neurelis, Inc. v. Padagis LLC et al.*, 1:24-cv-562, D.I. 88-28 (D. Del. August 22, 2025) ("Donovan-CC Decl.")
2070	Certified transcription of December 10-11, 2025, Volume I and II Deposition of Maureen Donovan, Ph.D. in *Padagis US LLC vs. Neurelis, Inc.*, IPR2025-00464, IPR2025-00465, IPR2025-00466 ("Donovan Transcript")
2071	*What is Log P and How Does It Predict Chemical Behavior?*, BIOLOGY INSIGHTS, (August 16, 2025), https://biologyinsights.com/what-is-log-p-and-how-does-it-predict-chemical-behavior/ ("Log P")
2072	NOT USED
2073	Declaration of Marc Brown regarding U.S. Patent No. 11,241,414
2074	NOT USED
2075	NOT USED
2076	Patent Owner Response, dated November 5, 2019 in *Aquestive Therapeutics, Inc. v. Neurelis, Inc.*, IPR2019-00451
2077	U.S. Patent No. 12,268,664 (the "'664 Patent")

Exhibit	Description of Exhibits
2078	Certificate of Correction for U.S. Patent No. 12,268,664
2079	Defendants' Notice of Non-Party Subpoenas, *Neurelis, Inc. v. Padagis LLC et al.*, 1:24-cv-562, D.I. 63 (D. Del. May 13, 2025)
2080	Non-Party Inventors' Responses to Subpoenas (D. Del. May 27, 2025)
2081	Email from Board (Nov. 18, 2025) authorizing moving Due Date 1 (highlighting added)
2082	IPR2025-00465, Paper 43, Petitioner's Reply to Patent Owner's Response (Mar. 31, 2026), with highlighting added to show portions that Patent Owner seeks to strike
2083	IPR2025-00465, Exhibit 1078, Reply Declaration of Maureen Donovan, Ph.D. (Mar. 31, 2026), with highlighting added to show portions that Patent Owner seeks to strike

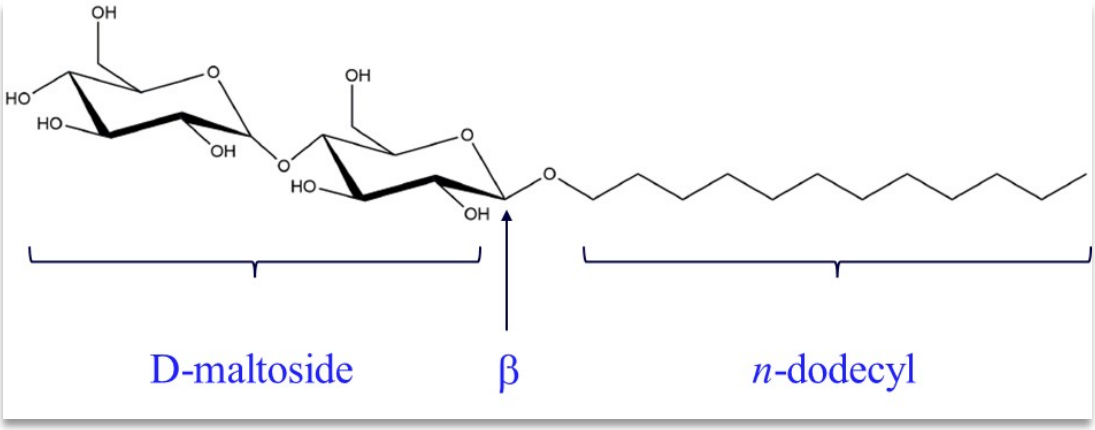
Neurelis ("PO") submits this Sur-Reply to Petitioner's Reply (Paper 43, "Reply").

I. COLLATERAL ESTOPPEL DOES NOT APPLY

A. ISSUES MATERIALLY DIFFER

Collateral estoppel does not apply when claims are "materially different" from those previously litigated. *ParkerVision, Inc. v. Qualcomm Inc.*, 116 F.4th 1345, 1356 (Fed. Cir. 2024); *MaxLinear, Inc. v. CF CRESPE LLC*, 880 F.3d 1373, 1377-78 (Fed. Cir. 2018) (remanding for failure to analyze dependent claims).

Every '414 Patent claim requires "*n*-dodecyl-β-D-maltoside," a single species with a linear alkyl chain:



In contrast, the sole independent claim of the '876 Patent (claim 1) recites a broad genus, "alkyl glycoside," and certain dependent claims (claims 26-28, 30-33) recite a broad subgenus, "dodecyl maltoside." EX2073 ¶¶184-185. There are numerous species of "dodecyl maltoside" due to glycosidic linkages (α, β), stereochemistry

(D, L), and the configuration of the dodecyl moiety (linear, branched). EX2073 ¶¶81, 186-190. No claim of the '876 Patent recites the "*n*-dodecyl-β-D-maltoside" present in every '414 Patent claim.

Petitioner's cited cases are inapposite. In *Ohio Willow Wood*, patent owner had "not provided any explanation regarding *how*" the difference in claim scope affects the invalidity analysis. *Ohio Willow Wood Co. v. Alps South, LLC*, 735 F.3d 1333, 1343 (Fed. Cir. 2013). In *Soverain*, the adjudicated claims recited a "network," while the unadjudicated claim recited, "the network is an Internet." "Routine incorporation of Internet technology … does not change the invalidity analysis." *Soverain Software LLC v. Victoria's Secret Direct Brand Mtmt., LLC*, 778 F.3d 1311, 1319-1320 (Fed. Cir. 2015). Here, differences in claim language materially affect patentability.

1. '414 Patent Priority Date

The difference between the '414 Patent requiring *n*-dodecyl-β-D-maltoside (species) and the '876 Patent requiring "alkyl glycoside" (genus) or "dodecyl maltoside" (subgenus) is material to priority date. "Whether a species is described adequately under 35 U.S.C. §112 versus whether a class/genera inclusive of the species is described are not identical inquiries." Paper 13 at 22. Petitioner ignores this point.

2. Obviousness over Gwozdz-PCT and Meezan

Obviousness requires a petitioner to demonstrate "that all claimed limitations are disclosed in the prior art." *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014). The uncontested presence of "alkyl glycoside" and "dodecyl maltoside" in prior art does not show disclosure of *n*-dodecyl-β-D-maltoside.[1] "[D]isclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus." *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006).

"Obviousness concerns whether a skilled artisan not only could have made but would have been motivated to make the combinations or modifications of prior art *to arrive at the claimed invention*." *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) (cleaned up). Meezan does not disclose the claimed *n*-dodecyl-β-D-maltoside (linear), but instead emphasizes the opposite, "highly branched alkyl glycosides including DDM" as preferred absorption enhancers.[2]

[1] The Petition failed to address prior art disclosure of "*n*-dodecyl-β-D-maltoside," so Petitioner resorted to new theories in Reply. Paper 48.

[2] This distinction is substantial because "highly branched alkyl chains including DDM" *are* within the scope of the '876 Patent claims, but *not* within the scope of the linear species in the '414 Patent claims.

EX2070 at 119:10-120:22, 138:23-141:2; EX2073 ¶¶189, 255, 258; EX1010 ¶[0149]. "[A] difference in the claims that would alter a POSITA's motivation to combine prior art references would be material to the invalidity analysis." *TQ Delta, LLC v. 2Wire, Inc*., 2021 WL 2671296 at *6 (D. Del. June 29, 2021). Petitioner disregards this case.

B. ISSUES WERE NOT ACTUALLY LITIGATED

Collateral estoppel also fails because it applies only to issues "actually litigated in the first action." *Google v. Hammond Development Int'l, Inc.*, 54 F.4th 1377, 1381 (Fed. Cir. 2022). Collateral estoppel does not apply to issues that merely "*could have been raised* in the prior litigation." *Purdue Pharma L.P. v. Iancu*, 767 F. App'x 918, 922 (Fed. Cir. 2019) (cleaned up) (original emphasis). Failure to contest an issue, or even stipulating to it, does not create collateral estoppel. *Id.*

1. Non-Obviousness over Gwozdz-PCT and Meezan

Petitioner suggests that because several dependent claims of the '876 Patent recited "dodecyl maltoside," issues pertaining to "*n*-dodecyl-β-D-maltoside" were litigated. Reply at 2-5. Petitioner is wrong.

IPR2019-00451 *nowhere addressed* whether the prior art discloses *n*-dodecyl-β-D-maltoside, as the '876 Patent did not claim it. In fact, in IPR2019-00451 patent owner did not contest whether the prior art disclosed any claim limitations, including "dodecyl maltoside." EX2076 at 28-29; EX1072 ¶¶76-77;

EX1040 at 27 ("Patent Owner does not present separate arguments for any of the dependent claims."). Nor did patent owner argue on appeal whether the prior art disclosed any of the claim limitations, or substantive non-obviousness of "dodecyl maltoside." EX1081 at 40-51.

2. '414 Patent Priority Date

Petitioner does not contend that IPR2019-00451 addressed priority of "*n*-dodecyl-β-D-maltoside." Rather, Petitioner contends IPR2019-00451 addressed dependent claims reciting "DDM" (dodecyl maltoside). Reply at 3 (citing EX1040 at 33-35, 37-47). These pages addressed obviousness, not priority date. The IPR2019-00451 panel did not address priority of "dodecyl maltoside"; rather, the panel stated that independent claim 1 is "illustrative of the challenged claims" and has "alkyl glycoside." EX1040 at 4-5, 14 n.6 ("Since all of the remaining claims of the '876 patent depend, directly or indirectly, from Claim 1, they also require the presence of 'an alkyl glycoside.'"), 19 n.7 ("alkyl glycoside"), 23 ("'558 provisional does not provide adequate written description support for the 'alkyl glycoside' limitation."); EX1072 ¶68 (expert declaration's section entitled, "The Provisional Application Incorporates by Reference Alkyl Glycosides as Claimed."); EX2076 at 24 ("POSA would have recognized and understood that alkyl glycosides were disclosed and supported").

Rather than address what the IPR2019-00451 panel determined, Petitioner points to "unsuccessful" appellate briefing and discussion of "dodecyl maltoside." Reply at 4 (citing EX1081). The Federal Circuit issued a Rule 36 summary affirmance; it too did not discuss priority of dodecyl maltoside (or *n*-dodecyl-β-D-maltoside). EX1068; *Hammond*, 54 F.4th at 1381 (requiring that an issue be "essential to a final judgment in the first action").

As this Panel noticed, the only suggestion of adequate written description for dodecyl maltoside "appears to have been relegated to a footnote," and petitioner argued that the issue had been waived. Paper 13 at 23-24; EX2028 at 51-52.

3. Priority of Gwozdz-PCT

In IPR2019-00451, "Patent Owner [did] not contest that Gwozdz[-PCT] is entitled to this filing date" of Gwozdz-Provisional. EX1040 at 14; Paper 13 at 34 n.18 ("Patent Owner's apparent concession that Gwozdz[-PCT] was prior art during the 451 IPR does not equate to the issue being actually litigated."). Petitioner does not address this argument, nor recent authority on priority-date analysis. Paper 28 ("POR") at 72; *In re Riggs*, 131 F.4th 1377, 1384 (Fed. Cir. 2025).

II. PETITIONER CONFLATES §103(c) PROVISIONS

Petitioner argues, "[w]ithout co-ownership, Section 103(c)(2) cannot apply." Reply at 14. While 35 U.S.C. §103(c)(1) (pre-AIA) requires actual co-ownership, §103(c)(2) does not. If the §103(c)(2) sub-provisions are met, subject matter

developed by another is "deemed to have been owned by the same person or subject to an obligation of assignment to the same person." Nevertheless, the §103(c)(2) argument is moot in this proceeding (subject to review and appeal) after the Board denied PO's motion for leave to amend the specification. Papers 36, 39.

III. GWOZDZ-PCT IS NOT PRIOR ART

Regarding priority date, Petitioner asserts: (1) a new argument in reply that the incorporation statement is not specific; (2) the Sigma catalog provides "essential material" and cannot be incorporated by reference; and (3) "blaze marks" caselaw applies. Petitioner is wrong.

A. THE SIGMA CATALOG IS INCORPORATED WITH PARTICULARITY

"To incorporate matter by reference, a host document must contain language 'clearly identifying the subject matter which is incorporated and where it is to be found.'" *Callaway Golf Co. v. Acushnet Co.*, 576 F.3d 1331, 1346 (Fed. Cir. 2009); 37 C.F.R. §1.57(c); *Novartis Pharm Co., v. Shilpa Pharma, Inc.*, IPR2022-00886, Paper 75 at 76 (P.T.A.B. Sep. 29, 2023).

The challenged incorporation identifies "biological detergents listed in the SIGMA Catalog, 1988, page 316-321 (which is incorporated herein by reference)." EX1008 ¶[152]. Such "unequivocal" language is proper. *Paice LLC v. Ford Motor Co.*, 881 F.3d 894, 908 (Fed. Cir. 2018); *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282-83 (Fed. Cir. 2000) ("host document must identify with

detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents"). The '558 Provisional names the publication, date, page numbers, and specific section of the reference that is incorporated. Both experts agree the Sigma Catalog was a well-known reference. EX2073 ¶¶178-179; EX2070 at 151:1-152:4, 179:8-12.

B. THE SIGMA CATALOG CAN BE INCORPORATED

Petitioner asserts Sigma Catalog is "essential material" and cannot be incorporated into the Provisional. Reply at 8-9. Petitioner is incorrect.

1. Petitioner Fails to Address *Acqis*

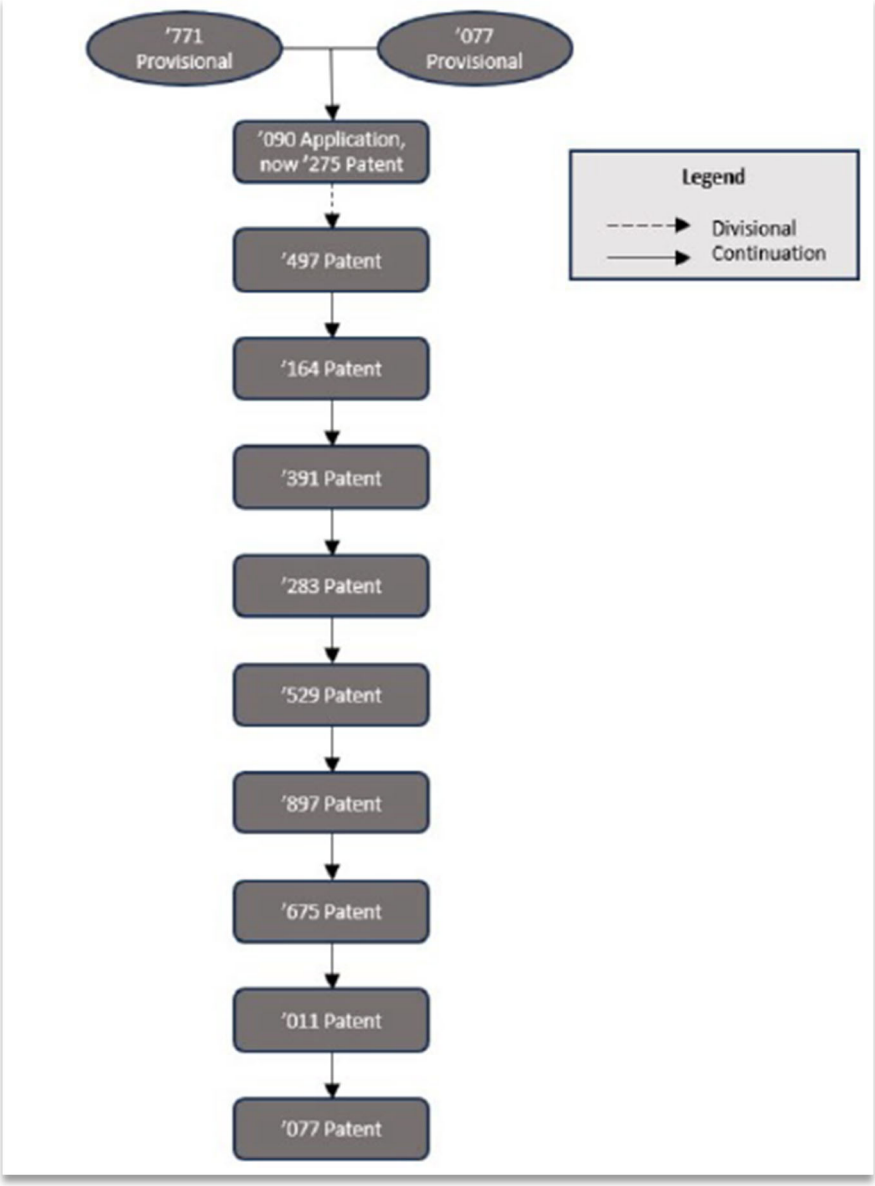
The "essential material" limitations of Rule 1.57(d) do not apply because provisionals are not required to have a "claimed invention" or include any patent claims. 37 C.F.R. §1.57(d)(1) (defining "essential material" as necessary to provide "a written description of the claimed invention"); 35 U.S.C. §111(b). "[W]hether certain disclosure is 'essential' depends entirely on what the claims recite in the particular application, not the claims in the later-filed application." *Samsung Electrons. Co. v. Acqis LLC*, IPR2021-00608, Paper 10 at 12 (P.T.A.B. Dec. 8, 2021) (cited by Paper 13 at 19 n.11).

2. Petitioner Fails to Address *Neurent* and M.P.E.P. §608.01(p)

"[L]imitations on the material which may be incorporated by reference in U.S. patent applications which are to issue as U.S. patents do not apply to applications

relied on only to establish an earlier effective filing date." M.P.E.P. §608.01(p)(I)(B). Thus, incorporating "nonpatent publications" or even "a U.S. patent or application which itself incorporates 'essential material' by reference … is not critical in the case of a 'benefit' application." *Id.*

Neurent followed M.P.E.P. §608.01(p)(I)(B). There, the challenged patent traced priority to the '090 Application:



Neurent Med. Inc. v. The Foundry, LLC, IPR2024-00669, Paper 8 at 16 (P.T.A.B. July 23, 2024). Although the Panel denied priority based on missing limitations, the Panel found "the introduction of subject matter from the '771 Provisional into the '893 Application, thereafter included in the '077 patent's Specification does not constitute new matter because the '090 Application incorporates by reference the

entirety of the '771 Provisional." *Id.* at 21-22. The panel permitted incorporation by reference of unpublished applications for priority and copying the contents into downstream applications.

Here, the '414 Patent and each parent claims priority to the '558 Provisional and incorporates by reference the Sigma Catalog. As in *Neurent*, the fact that "the first non-provisional application filed from the '558 provisional" expressly copies some of the species from the Sigma Catalog (Reply at 10) does not defeat priority. 37 C.F.R. §1.57(g); EX1039.

3. Sigma Catalog Is Not Necessary to Provide Written-Description Support

The originally-filed '414 Patent claims expressly recited "*n*-dodecyl beta-D-maltoside." EX1002 at 268-70, cl. 1. "Original claims are part of the original specification and in many cases will satisfy the written description requirement." *Mentor Graphics Corp. v. EVE-USA, Inc.*, 851 F.3d 1275, 1297 (Fed. Cir. 2017). Thus, the Sigma Catalog and Provisional are unnecessary for written description of the '414 Patent claims, but instead are "relied on only to establish an earlier effective filing date." M.P.E.P. §608.01(p)(1)(B).

According to Petitioner, the "*n*-" prefix in *n*-dodecyl-β-D-maltoside "is neither necessary nor used to identify or name straight-chain alkanes." EX1078 ¶¶15-18, 40-42. Dr. Donovan now contends "Meezan expressly discloses 'dodecyl-

β-D-maltoside,' [which] a POSA would have understood that to be a reference to 'n-dodecyl-β-D-maltoside.'" EX1078 ¶39. If it is sufficient under Dr. Donovan's theory for Meezan to disclose "dodecyl-β-D-maltoside" (without the "*n*-"), then the '414 Patent and its parent applications do as well, as their specifications have this same "dodecyl-β-D-maltoside" language. EX2073 ¶141 (discussing disclosures of EX1039, EX1003, and EX1001); *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2010) ("specification itself that must demonstrate possession" but need not "recite the claimed invention *in haec verba*"). The Sigma Catalog is not necessary to provide written-description support for the '414 Patent or its non-provisional parent applications, as the specifications themselves provide this support. There are no limitations precluding the Provisional or downstream applications from incorporating the Sigma Catalog. M.P.E.P. §608.01(p)(I)(B).

C. THE '558 PROVISIONAL PROVIDES SUFFICIENT SUPPORT

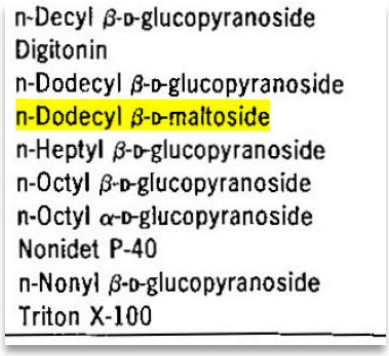
1. Blaze Marks Are Not Required

As PO described and Petitioner ignores, *Fujikawa* and *Purdue Pharma* address Markush groups where a genus or sub-genus was disclosed and a species was claimed. POR at 27-28. These cases do not apply here, where "[t]he claims are narrow" in that they "recite specific ingredients … not classes of ingredients." *Allergan USA, Inc. v. MSN Lab'ys Priv. Ltd.*, 111 F.4th 1358, 1372 (Fed. Cir. 2024);

POR at 28-29. The '414 Patent recites the claimed compound *n*-dodecyl-β-D-maltoside and does not require blaze marks to find it.

2. The '558 Provisional Provides Blaze Marks

The Sigma Catalog discloses *n*-dodecyl-β-D-maltoside *in haec verba* on the first page the '558 Provisional cites. POR at 25-26.


n-Decyl β-D-glucopyranoside
Digitonin
n-Dodecyl β-D-glucopyranoside
n-Dodecyl β-D-maltoside
n-Heptyl β-D-glucopyranoside
n-Octyl β-D-glucopyranoside
n-Octyl α-D-glucopyranoside
Nonidet P-40
n-Nonyl β-D-glucopyranoside
Triton X-100

EX1026 at 19. This is not the "broad reference" found in *Regents*, where it was "unclear how many compounds actually fall within the described genera and subgenera." *Regents of the Univ. of Minn. v. Gilead Sciences, Inc.*, 61 F.4th 1350, 1357 (Fed. Cir. 2023). Rather, the Sigma Catalog has a finite list of biological detergents that a POSITA would understand to disclose *n*-dodecyl-β-D-maltoside. EX2070 at 178:9-179:7 (agreeing that a POSITA would "immediately discern" the disclosure of *n*-dodecyl-β-D-maltoside in the Sigma catalog); EX2073 ¶¶179-183.

IV. THE CHALLENGED CLAIMS ARE NOT OBVIOUS

The combination of Gwozdz-PCT/Meezan does not render obvious any claims. First, the combination does not disclose all claim limitations. Second,

Petitioner fails to present a compelling reason why a POSITA would combine the two references, while ignoring the numerous reasons dissuading from such a combination. Petitioner's obviousness rationales are rife with hindsight.

A. FAILURE TO DISCLOSE OR SUGGEST ALL CLAIM LIMITATIONS

"[P]etitioner has the burden from the onset to show with particularity with the patent it challenges is unpatentable." *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016). "[A]n entirely new theory of prima facie obviousness" cannot be raised in reply, even if it "is responsive to the patent owner's response." *Corephotonics, Ltd. v. Apple Inc.*, 84 F.4th 990, 1008 (Fed. Cir. 2023); Paper 48 at 5-7. It is not permissible for a reply to include "previously unidentified portions of a prior-art reference to make a meaningfully distinct contention" and cite "several new non-patent literature references" to support obviousness opinions. *Apple Inc. v. Andrea Elecs. Corp.*, 949 F.3d 697, 706 (Fed. Cir. 2020). Here, Petitioner introduces new evidence and theories.

1. No Disclosure or Suggestion of *n*-dodecyl-β-D-Maltoside

Every challenged claim recites *n*-dodecyl-β-D-maltoside, which differs from "dodecyl maltoside." EX2073 ¶¶ 81, 205; EX1077, 71:14-18. The Petition failed to identify any disclosure of *n*-dodecyl-β-D-maltoside in Gwozdz-PCT or Meezan. POR at 40-43. For Claim Element 1(d), the Petition includes one conclusory

paragraph directed to the broader genera of "alkyl glycosides, including dodecyl maltoside." Petition at 39 (citing EX1062 ¶136).

Dr. Donovan's opening declaration does not mention "linear" or identify any disclosure of *n*-dodecyl-β-D-maltoside. Rather, she quotes passages describing "highly branched alkyl chains" for "the alkyl glycoside … to be utilized in the compositions"—the opposite of the claimed linear species. EX1062 ¶92 (citing EX1010 ¶[0149]). She did not understand the meaning of the *n*- prefix in *n*-dodecyl-β-D-maltoside and "what structural information" it conveys. EX2070 at 193:2-25.

a. Petitioner Belatedly Applies IUPAC Naming

To fill this hole in the prior art, Petitioner adds new evidence to reinterpret Meezan. Reply at 14-16. Petitioner alleges that under IUPAC naming conventions, "straight chain alkanes need no prefix, including no 'n-' prefix." Reply at 14. Petitioner's only support for this statement is Dr. Donovan, who previously testified she did not know what this prefix meant. She apparently did further research and, for the first time, cites snippets of an IUPAC book. EX1078 ¶18 (citing EX1079). The Board should disregard this new IUPAC theory.

First, EX1079 is not properly in evidence as it was first filed with Petitioner's Reply brief, but then not even cited. Petitioner failed to provide "a detailed explanation of the significance of the evidence." 37 C.F.R. §42.104(b)(5).

Second, neither Petitioner nor Dr. Donovan point to anything that actually says the "*n*-" prefix is optional when naming chemical compounds. EX1078 ¶18 (citing EX1079 at 4-6). EX1079 does not mention the "*n*-" prefix or provide any guidance in naming glycosides or other chemical compounds beyond hydrocarbons and homogenous hydrides. EX1079 at 4-6. Dr. Donovan fails to explain how EX1079 supports her position, and Petitioner does not even cite EX1079.

Third, this argument lacks relevance. There is no indication Gwozdz-PCT, Meezan, or the challenged patent referred to or adhered to IUPAC naming conventions. The patent claims "*n*-dodecyl-β-D-maltoside," so either the '414 Patent was not using IUPAC naming conventions (under Donovan's view), or IUPAC naming conventions do not preclude the "*n*-" prefix.

Fourth, "prior art must be considered for all its teachings, not selectively." *Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1332 (Fed. Cir. 2019). Meezan describes the structure of dodecyl maltoside as "highly branched" (the opposite of "*n*-") and declines to use IUPAC naming conventions. EX1010 ¶[0149]. Petitioner and Dr. Donovan disregard the teachings of Meezan and seek to retroactively impose a standard that Meezan did not follow.

As Dr. Brown opines, naming chemical compounds is "dependent on the environment at which you're discussing them and the context thereof." EX1077 at 94:24-95:5, 97:8-22. For example, a butane lighter can be filled with *n*-butane, *iso*-

butane, or both.[3] EX2073 ¶70. Similarly, "dodecyl" can refer to many arrangements of 12 carbon atoms, whether linear or branched. EX2073 ¶¶81, 187, 209. The '414 Patent claims a specific chemical compound with a specific structure. Meezan lacks the requisite specificity and does not describe the claimed compound.

b. Meezan Teaches the Opposite of the Claimed Compound

The only location where Meezan describes the isomeric structure of dodecyl maltoside (DDM) identifies "***highly branched*** alkyl chains including DDM." EX1010 ¶[0149]; EX2073 ¶¶258-259. This is the same paragraph that the Petition and Dr. Donovan rely on for the disclosure of dodecyl maltoside. Petition at 39-40; EX1062 ¶92. Dr. Donovan admitted that in Meezan, "there is nothing that indicates … any specifics about arrangement of the alkyl chain," other than this passage referring to "highly branched." EX2070 at 99:19-21, 119:10-120:22, 138:23-141:2. Petitioner does not dispute that the challenged claims are limited to the linear isomer

[3] Petitioner relies on an undergraduate textbook, but even that refers to "*n*-alkanes." EX1077 at 94:13 (discussing EX2051). As Dr. Brown opines, "textbooks [have] … general descriptions of alkanes, such as *n*, *iso*, and …*neo*. …It just depends upon the context that you're using them." EX1077 at 91:12-16.

(Reply at 14-16), but ignores that the compounds Meezan discloses for "dodecyl maltoside" are "highly branched," not "linear."

c. New Evidence Does Not Support Obviousness

Dr. Donovan attempts to backfill the Petition by re-writing Meezan. She introduces a new exhibit, purportedly from Meezan's prosecution history, that unsuccessfully sought to amend the specification. EX1078 ¶¶46-47 (citing EX1075 at 6). EX1075 was not cited in the Petition, is not a patent or printed publication under 37 C.F.R. §42.104(b)(2), and is not part of the Meezan publication. *Apple Inc. v. DoDots Licensing Solutions LLC*, IPR2023-00939, Paper 12 at 15-17 (P.T.A.B. Jan. 3, 2024) (declining to consider documents within the file history of a reference, "as they are not part of the patent" and not prior art). Meezan was abandoned and the purported amendment was never approved. EX1075 (supplemental) at 193.[4] An abandoned amendment never included in the printed publication cannot override the "highly branched" language used in the actual prior art reference.

Petitioner's reliance on a hearsay declaration of Ed Maggio, buried in the file history of a different patent, is also unavailing. Reply at 16-17. Exhibit 1076 was signed in 2013, over seven years after Meezan's 2006 publication date (EX1010) and four years after the '414 Patent's priority date. This "new theory of invalidity

[4] Petitioner served the full prosecution history of EX1075 as supplemental evidence.

by reference to new evidence" introduced in reply should be stricken. *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016).

d. No Motivation Toward *n*-dodecyl-β-D-maltoside

Petitioner fails to find disclosure of *n*-dodecyl-β-D-maltoside in the asserted references and also does not establish motivation to combine.

Petitioner cites a single example, Meezan ¶[0157], which compares dodecyl maltoside (DDM), tridecyl maltoside, and tetradecyl maltoside (TDM) as "absorption enhancers for ocular administration of insulin" through ocular routes (eyedrops). Reply at 26. The same paragraph describes TDM as having "the greatest effect," but Petitioner ignores this and focuses on DDM (which is not the claimed compound). Reply at 26; EX1010 ¶[0157].

The *Fulton* case cited by Petitioner is inapposite. *Fulton* suggests that the "desirability of a particular combination need not be supported" by a preferred combination in the prior art. *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004). But in *Fulton* there were no other prior art findings that taught away from the "less desirable" combination. Meezan expresses a distinct preference for TDM and "highly branched" compounds. *N*-dodecyl-β-D-maltoside is neither.

Petitioner ignores the full scope of Meezan and reviews Table I in a vacuum. A POSITA would look at all the Examples disclosed in Meezan and see that there is a quantifiable advantage of TDM over DDM. EX2073 ¶¶267-270. In Table III,

decyl maltoside, dodecyl sucrose, and tridecyl maltoside all outperformed DDM at the same 0.5% concentration for decreasing the amount of blood glucose via eyedrops (not intranasal) in rats. EX2073 ¶269. Table II shows that that 0.125% TDM eye drops were more effective than DDM. EX2073 ¶267. In short, nothing in Meezan suggests the desirability of using dodecyl maltoside in intranasal applications (as compared to TDM); nor does anything disclose or even suggest the use of the linear species, as opposed to "highly branched."

2. No Disclosure or Suggestion of Non-Aqueous Solutions

Petitioner failed to explain how the prior art meets the "consisting of" limitation when the Petition relied on aqueous embodiments of the prior art. POR at 43-45. Even after abandoning its previous claim-construction positions and relying on new embodiments, Petitioner still cannot demonstrate this limitation.

a. Petitioner's Improper Claim Construction Tactics

The challenged claims require a formulation "consisting of" various elements, none of which is water. In district court, Petitioner narrowly construed "consisting of" to mean either the claims must exclude all water or the claims are indefinite. EX2050 at 27, 46, 53-57. Dr. Donovan prepared a declaration espousing this very position. EX2069 ¶¶26, 33, 50, 53, 57.

The Petition did not identify these constructions. Every prior art embodiment the Petition cites explicitly contains water. POR at 43-45. For example, the Petition

cites "other pharmaceutically acceptable additives" in Gwozdz-PCT as supplying motivation to combine. Petition at 22, 27, 30, 39. This embodiment is expressly aqueous, in "saline solution or water." EX1009 at 10:2-16. Petitioner sought "broader constructions at the Board to support a patentability challenge while seeking narrower constructions in litigation to avoid infringement liability." *Revvo Techs., Inc. v. Cerebrum Sensor Techs., Inc.*, IPR2025-00632, Paper 20 at 4 (P.T.A.B. Nov. 3, 2025) (precedential).

Faced with this inconsistency and failure to address the scope of "consisting of" in prior art, Petitioner changes horses. The day before filing Petitioner's Reply, Petitioner unilaterally filed a "stipulation" in district court to withdraw its claim-construction position. EX1083. Dr. Donovan also asks the Board to ignore her district court declaration. EX1078 ¶¶32-33.

First, the rules do not permit parties to assert inconsistent claim constructions. Second, Petitioner now asserts new theories for how the prior art is non-aqueous (discussed below). Third, as Petitioner knows, at least one co-defendant has *not* offered such a stipulation and pursues the same argument based on "consisting of." Such gamesmanship is not permitted.

Petitioner violated 37 C.F.R. §42.104(b)(3), which "requires ***a petition*** to identify '[h]ow the challenged claim is to be construed.'" *Tesla, Inc. v. Intellectual Ventures II LLC*, IPR2025-00340, Paper 18 at 2 n.1 (P.T.A.B. Nov. 5, 2025)

(informative). Petitioner states that "[i]n the litigation, Petitioner agreed to Patent Owner's proposed construction" of "no construction necessary" (Reply at 7), but this "does not explain sufficiently why the different positions were warranted." *Revvo*, IPR2025-00632, Paper 20 at 5 (rejecting excuse that petitioner "accepts Patent Owner's proposed constructions").

b. Petitioner Shifts to New Theories in Reply

Petitioner pivots to a new embodiment of Gwozdz-PCT as purportedly teaching non-aqueous intranasal solutions. Reply at 19, 23-24 (citing EX1009 at 11:17-26); EX1078 ¶11. This embodiment was not cited in the Petition and is improper in reply. *Ariosa Diagnostics v. Verinata Health, Inc.*, 805 F.3d 1359, 1367 (Fed. Cir. 2015) ("Not until … Reply declaration did Ariosa identify specific embodiments … that do not use restriction-enzyme digestible primers."); *Corephotonics*, 84 F.4th at 1009 (reply is improper if it "'point[s] to any new embodiments' of a prior art reference not previously identified in the petition"). This new embodiment does not demonstrate obviousness.

c. No Motivation to Combine

The newly cited embodiment of Gwozdz-PCT states, "Formulations suitable for parenteral administration can be aqueous or non-aqueous ***injection*** solutions." EX1009 at 11:17-19; Reply at 19, 23-24. An injection embodiment definitionally provides "absolute or 100% bioavailability." EX2073 ¶109 (i.e., injections serve as

the benchmark for bioavailability measurements). But according to the Petition, the motivation to combine Gwozdz-PCT and Meezan is for "improved bioavailability." Petition at 30-32. If the new embodiment from Gwozdz-PCT is already 100% bioavailable (i.e., an injection), there would be no reason to modify Gwozdz-PCT with Meezan, as Gwozdz-PCT already provides 100% bioavailability.

The hindsight continues: every example in Meezan is directed to adding alkyl glycosides to aqueous solutions of peptides or proteins. EX2073 ¶216. Against the weight of disclosure, Petitioner cites the singular instance of the word "non-aqueous," found in a boilerplate catch-all paragraph of Meezan. Reply at 19 (citing EX1010 ¶[0074]). Petitioner is improperly "us[ing] hindsight reconstruction to pick and choose among isolated disclosures to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1998); *Fulton*, 391 F.3d at 1200 ("whether there is something in the prior art as a whole to suggest the *desirability*, and thus the obviousness, in making the combination available").

Petitioner relies on a different passage of Meezan for its disclosure of DDM. Reply at 26 (citing EX1010 ¶[0157]). But this passage discloses "ocular [eyedrops]

administration of insulin" (a macromolecule), not intranasal administration of diazepam (small molecule).[5] EX1010 ¶[0157].

*****

To reconstruct the challenged claims, requiring a non-aqueous intranasal solution of *n*-dodecyl-β-D-maltoside and diazepam, Petitioner starts with an injection solution of benzodiazepines in Gwozdz (EX1009 at 11:17-26) that definitionally has 100% bioavailability. Petitioner modifies that solution by combining with an embodiment of Meezan directed to aqueous insulin eye drops, while simultaneously relying on a "non-aqueous" boilerplate statement. This is unbridled hindsight.

B. PETITIONER'S GENERIC MOTIVATIONS DO NOT ESTABLISH OBVIOUSNESS

Petitioner generically asserts that a "POSA developing pharmaceutical dosage forms would still seek better solubility, stability, and bioavailability." Reply at 20. This argument reduces to the truism that nothing is perfect, and any formulation can always be better. EX1077 at 129:2-16. But that is not the law. *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1327-1328 (Fed. Cir.

[5] The molecular weight of insulin is 5,800 Daltons, compared to diazepam's 285 Daltons. EX1077 at 214:12-17; EX2073 ¶246.

2012) (generic testimony "fails to explain why a person of ordinary skill in the art would have combined elements from specific references *in the way the claimed invention does*."); *Pers. Web Techs., LLC v. Apple, Inc.*, 848 F.3d 987, 992 (Fed. Cir. 2017) (rejecting rationale that a POSITA "once presented with the two references, would have understood that they *could* be combined"). None of Petitioner's generic solubility, stability, and bioavailability theories pass muster.

1. Gwozdz-PCT Solves the Problem of Bioavailability

As discussed above, the aqueous embodiments cited from Gwozdz-PCT (injectables) are already 100% bioavailable. Thus, bioavailability cannot provide any motivation. EX1009 at 7:5-8 (Gwozdz-PCT already "provid[es] increased bioavailability of the therapeutic agent").

2. Gwozdz-PCT Solves the Problem of Solubility

Petitioner relies on the patent itself to frame the problem of solubility. POR at 46. Petitioner responds with the non-sequitur that PO denies the existence of solubility problems in prior art other than Gwozdz-PCT. Reply at 20. The issue is that Petitioner employs "hindsight reconstruction by using the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit." *In re NTP, Inc.*, 654 F.3d 1279, 1299 (Fed. Cir. 2011) (cleaned up).

Petitioner fails to respond to the fact that Gwozdz-PCT already solved the problem. Reply at 20. Absent evidence, Petitioner speculates that a "POSA … would still seek better solubility." Reply at 20. But Petitioner identifies no shortcomings in Gwozdz-PCT or need for improvement. Petitioner has not demonstrated that its "[f]ormulation of the problem was derived directly from the prior art, rather than from the challenged claims." *Purdue Pharma L.P. v. Depomed, Inc.*, 643 F. App'x 960, 966 (Fed. Cir. 2010).

3. The Combination Does Not Improve Stability

Petitioner does not dispute that its own exhibits demonstrate negative interactions between benzyl alcohol, ethanol, and *n*-dodecyl-β-D-maltoside. Instead, Petitioner contends without any evidence (other than Dr. Donovan's unsupported musings) that these interactions "would not deter a POSA." Reply at 21. The '414 claims are not limited to "a one-time use product," as Petitioner contends, which might otherwise minimize these concerns. *Medtronic, Inc. v. Teleflex Innovations S.a.r.l.*, 69 F.4th 1341, 1349 (Fed. Cir. 2023) (POSITA would consider whether "a proposed modification would interfere with a reference's stated purpose"). Petitioner ignores this case. Nor does Petitioner acknowledge that ethanol was already a known penetration enhancer, to which a POSITA would not have been motivated to add a second one. POR at 51.

Tocopherols were known to be unstable. EX2070 at 283:18-284:13. Petitioner's replies that "Gwozdz[-PCT] itself teaches formulations containing one or more tocopherols" and that other ingredients may be added. Reply at 22. But given the stability issues of tocopherols, a POSITA would have been dissuaded from modifying a working formulation absent a compelling reason. EX2073 ¶¶82-88, 250-254 (citing EX2053-EX2059). Petitioner's reference to tocopherols with "additional pharmaceutically acceptable additives" appears in the embodiment on injection applications, not nasal administrations, and Meezan fails to teach any application to tocopherol-based solutions. POR at 57.

*****

At bottom, nothing would have motivated a POSITA to improve Gwozdz-PCT, let alone with the disclosures of Meezan. Petitioner's asserted motivation to combine reduces to: any pharmaceutical solution can always be made better. Such a generalized desire to improve prior-art formulations does not establish a reason to combine prior-art elements "in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007); *Virtek Vision Int'l ULC v. Assembly Guidance Sys., Inc.*, 97 F.4th 882, 887 (Fed. Cir. 2024) ("mere fact that these possible arrangements existed in the prior art does not provide a reason that a skilled artisan would have" made the combination).

C. PETITIONER'S RELIANCE ON "OTHER PHARMACEUTICALLY ACCEPTABLE ADDITIVES" AND "WETTING AGENTS"

The "penetration enhancer" embodiment is not prior art because it does not appear in Gwozdz-Provisional (EX1064). POR at 52-53. Petitioner does not dispute this. Reply at 12. Instead, Petitioner switches to Gwozdz's "wetting … materials" as an alleged motivation. Reply at 23; EX1009 at 10:9-16. This is a new theory, impermissible in reply.

Also, the "wetting … materials" disclosure, like "other pharmaceutically acceptable additives," appears in the embodiment on injection application, but not in the section for "nasal applications." EX1009 at 9:19-10:2, 10:3-16. The route of administration is an important factor in drug delivery, which Petitioner ignores. EX1077 at 140:19-142:3. Petitioner also ignores the purpose of a "wetting" agent, which "modifies interfacial tension of water." EX1010 ¶[0053]. Petitioner relies on *aqueous* injections as its motivation to combine to arrive at *non-aqueous* intranasal applications. This is another example of improper hindsight reconstruction. *Henny Penny*, 938 F.3d at 1332 ("[P]rior art must be considered for all its teachings, not selectively").

D. MEEZAN IS DIRECTED TO MACROMOLECULES AND DOES NOT ADDRESS COMPATIBILITY WITH TOCOPHEROL SOLUTIONS

Petitioner asserts that a single disclosure of "small organic molecules" would teach a POSITA that Meezan could be applied to small molecules. Reply at 24-25.

Not so. A POSITA must "read the whole … document to understand what [Meezan] mean[s] by small organic drug molecules." EX1077, 154:6-8; POR at 55-56; *In re Fine*, 837 F.2d at 1075 (do not "pick and choose among isolated disclosures in the prior art to deprecate the claimed invention"). Petitioner does not identify any examples of small molecule applications in Meezan.

Petitioner does not respond to why a POSITA would even consider Meezan for small molecules, nor to the cases that PO cites regarding no motivation to combine when there are redundant effects. POR at 56-57.

Petitioner also claims that Meezan's compounds may be used in aqueous or non-aqueous solutions. Reply at 25. As stated and unrefuted by Petitioner, all of Meezan's examples combine a disclosed compound in aqueous solutions of peptide or proteins (i.e., macromolecules). POR at 57-58. Petitioner is also still silent on the incompatibility of the Meezan compounds with tocopherol-containing solutions. POR at 57 (citing EX2070 at 149:7-150:7; EX2073 ¶249). Petitioner does not and cannot reconcile any disclosure of tocopherol-containing solutions like those of Gwozdz-PCT with that of Meezan. POR at 57.

V. CONCLUSION

Petitioner has failed to meet its burden of proving unpatentability of any '414 Patent claims.

Dated: May 12, 2026

/David J. Tobin/

David J. Tobin
(Reg. No. 60,776)
MCDERMOTT WILL & SCHULTE LLP
2801 North Harwood Street, Suite 2600
Dallas, TX 75201
Tel: (214) 210-2793
dtobin@mcdermottlaw.com

Counsel for Patent Owner

CERTIFICATION OF WORD COUNT

The undersigned hereby certifies that the portions of the above-captioned PATENT OWNER'S SUR-REPLY, contain 5,582 words, in compliance with the 5,600 word limit set forth in 37 C.F.R. § 42.24(c)(4). This word count was prepared using Microsoft Word 365 V.2503.

Dated: May 12, 2026

/David J. Tobin/

David J. Tobin
(Reg. No. 60,776)
MCDERMOTT WILL & SCHULTE LLP
2801 North Harwood Street, Suite 2600
Dallas, TX 75201
Tel: (214) 210-2793
dtobin@mcdermottlaw.com

Counsel for Patent Owner

CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing PATENT OWNER'S SUR-REPLY was served on counsel of record for the Petitioner by filing this document through PTAB P-TACTS and by sending the same via electronic mail to the following addresses:

James P. Murphy
Reg. No. 55,474
Polsinelli PC
1000 Louisiana Street
Suite 6400
Houston, Texas 77002
Tel: (713) 374-1600
jpmurphy@polsinelli.com

Corey Casey
Reg. No. 66,950
Polsinelli PC
900 West 48th Place
Suite 900
Kansas City, Missouri 64112
Tel: (816) 572-4439
ccasey@polsinelli.com

Mark Deming
Reg. No. 69,263
Polsinelli PC
150 N. Riverside Plaza Suite 300
Chicago, IL 60606
mdeming@polsinelli.com

Chad A. Landon
Provisionally Recognized Pro Hac Vice
Polsinelli PC
1401 I St. NW Suite 800
Washington, DC 20005
clandmon@polsinelli.com

Dated: May 12, 2026

/David J. Tobin/
David J. Tobin
(Reg. No. 60,776)
MCDERMOTT WILL & SCHULTE LLP
2801 North Harwood Street, Suite 2600
Dallas, TX 75201
Tel: (214) 210-2793
dtobin@mcdermottlaw.com

Counsel for Patent Owner