

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. FALK PHARMA GMBH,
Petitioner,

v.

ELLODI PHARMACEUTICALS, L. P.,
Patent Owner.

Case No. IPR2025-00055
Patent No. 9,486,407

PATENT OWNER'S RESPONSE

Table of Contents

	Page
I. INTRODUCTION	1
II. THE GROUNDS	2
III. BACKGROUND	6
A. The '407 Patent (EX1001)	6
IV. THE LEVEL OF ORDINARY SKILL IN THE ART	8
V. CLAIM CONSTRUCTION	8
VI. PETITIONER FOCUSES ON IRRELEVANT BACKGROUND PRIOR ART	8
A. The Budesonide Prior Art Either Cannot Deposit Budesonide on the Upper Gastrointestinal Tract or uses Dohil's 8-12mL Liquid	9
VII. PETITIONER'S ANALYSIS OF THE PRIOR ART IS GUIDED BY IMPERMISSIBLE HINDSIGHT	11
A. Dohil	11
B. Grother	15
C. Singh and Cherukuri	18
D. FDA Guidance	18
E. Starting with an ODT when Solving the Problem of Delivering Topically Acting Corticosteroid to Upper Gastrointestinal Tract is Impermissible Hindsight	19
VIII. THE EPO DECISION DOES NOT CONTROL	22
IX. THE CLAIMS OF THE '407 PATENT ARE PATENTABLE	24
A. It was Not Obvious to Formulate ODT to Topically Deposit a Corticosteroid on the Upper Gastrointestinal Tract and treat EoE	24
1. Dohil Does Not Suggest or Teach ODTs as Required by Claims 1-4, 16-19, 21-23, and 35-39	24
2. Dohil Provides No Motivation to Formulate an ODT	28

Table of Contents
(continued)

	Page
a. Venkatesh Does Not Cure the Deficiencies in Dohil	33
b. No Expectation of Success in Arriving at the Claimed Invention	36
c. Dohil Does Not Disclose the Claimed Doses in the Context of a Tablet (Claims 1[ii], 35[i], 33-34)	38
a. Dohil Does Not Teach or Suggest the Claimed Methods for Treatment (Claims 1-4, 16-19, 21-23)	39
a. Dohil and Venkatesh Do Not Render Obvious Claims 5-15, 20	40
B. Grother and the FDA Guidance do Not Render the Claimed ODT Obvious	41
1. Grother and the FDA Guidance are General References and Do Not Teach or Suggest the ODT as Required By Claims 1-4, 16-19, 21, 23-25, 27-42	41
2. No motivation to formulate the claimed ODT based on Grother in view of the FDA Guidance – No Recognition that an ODT could topically deposit a corticosteroid on the Upper Gastrointestinal Tract	43
a. Venkatesh does Not Cure the Deficiencies in Grother and the FDA Guidance	46
b. Grother and the FDA Guidance Do Not Render Obvious the Claimed Doses (Claims 1[ii], 35[i], 33-34)	50
b. Grother Does Not Disclose the Claimed Methods for Treatment (Claims 1-4, 16-19, 21, 23-25, 27-34)	51
a. Grother, the FDA Guidance and Venkatesh Do Not Render Obvious Claims 5-15, 20, 26	52
X. OBJECTIVE INDICIA OF NONOBVIOUSNESS	53
A. Unexpected Results	53

Table of Contents
(continued)

	Page
XI. CONCLUSION.....	55

Table of Authorities

Page(s)

TABLE OF AUTHORITIES

Page(s)

Cases

<i>Apple Inc. v. Corephotonics, Ltd.</i> , Case IPR2018-01348, 2019 WL 3714167 (P.T.A.B. Aug. 5, 2019).....	44
<i>Boston Sci. Scimed, Inc. v. Cordis Corp.</i> , 554 F.3d 982 (Fed. Cir. 2009)	44
<i>In re Cyclobenzaprine</i> , 676 F.3d 1063 (Fed. Cir. 2012)	30
<i>DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.</i> , 567 F.3d 1314 (Fed. Cir. 2009)	33
<i>Dr. Falk Pharma GMBH v. Ellodi Pharma. L.P.</i> , IPR2024-01197	3, 20, 32
<i>Dr. Falk Pharma GmbH v. Ellodi Pharms., L.P.</i> , IPR2024-01197, Paper 20 (P.T.A.B July 14, 2025).....	32
<i>In re Fritch</i> , 972 F.2d 1260 (Fed. Cir. 1992)	35
<i>In re Gordon</i> , 733 F.2d 900, USPQ 1125 (Fed. Cir. 1984)	32
<i>Interconnect Planning Corp. v. Feil</i> , 774 F.2d 1132 (Fed. Cir. 1985)	20, 29
<i>Knoll Pharm. Co. v. Teva Pharms. USA, Inc.</i> , 367 F.3d 1381 (Fed. Cir. 2004)	22
<i>LG Display Co. v. Innovative Display Techs. LLC</i> , Case IPR2014-01362, Paper 12 (P.T.A.B. Mar. 2, 2015)	45

Table of Authorities
(continued)

	Page(s)
<i>In re Magnum Oil Tools Int’l, Ltd.</i> , 829 F.3d 1364 (Fed. Cir. 2016)	36, 46, 48, 51
<i>Medtronic, Inc. v. Daig Corp.</i> , 789 F.2d 903 (Fed. Cir. 1986)	23
<i>Metalcraft of Mayville, Inc. v. The Toro Co.</i> , 848 F.3d 1358 (Fed. Cir. 2017)	29
<i>Plas-Pak Indus., Inc. v. Sulzer Mixpac AG</i> , 600 F. App’x 755 (Fed. Cir. 2015)	35
<i>In re Ratti</i> , 270 F.2d 810, 123 USPQ 349 (C.C.P.A. 1959).....	32, 35
<i>Smith & Nephew, Inc. v. ConvaTec Techs. Inc.</i> , IPR2013-00097, Paper 76 (P.T.A.B. Feb. 24, 2014).....	23
Other Authorities	
37 C.F.R. § 42.104(B)(4)	4
FDA Guidance for Industry: Orally Disintegrating Tablets (2008)	4
MPEP	
§ 2143.01 (IV).....	32
§ 2143.01 (V)	31

List of Patent Owner's Exhibits

Exhibit No.	Description
2002	Dellon, E.S. et al., Fluticasone Propionate Orally Disintegrating Tablet (APT-1011) for Eosinophilic Esophagitis: Randomized Controlled Trial, Clinical Gastroenterology and Hepatology 20:2485–2494 (2022)
2003	Excerpt from the file history of U.S. Patent No. 10,632,069
2004	Transcript of the August 29, 2025 Deposition of Alan F. Parr, Pharm.D., Ph.D. from Nos. IPR2025-00052, IPR2025-00054, and IPR2025-00055
2005	Iorgulescu, G., Saliva between normal and pathological. Important factors in determining systemic and oral health, Journal of Medicine and Life Vol. 2, No.3, July-September 2009, pp.303-307
2006	Miehkle, S. et al., A randomised, double-blind trial comparing budesonide formulations and dosages for short-term treatment of eosinophilic oesophagitis, Gut 0:1-10 (2015)
2007	Declaration of Martyn Christopher Davies in Support of Patent Owner's Response
2008	<i>Curriculum Vitae</i> of Martyn Christopher Davies
2009	<i>Reserved</i>
2010	Clinical Trials Study, "Efficacy, Safety, and Pharmacokinetics of APT-1011 in Subjects With Eosinophilic Esophagitis (EoE)(FLUTE)," last updated Apr. 26, 2023, https://clinicaltrials.gov/study/NCT03191864?tab=results&a=11#outcome-measures
2011	Transcript of the April 9, 2025 Deposition of Alan F. Parr, Pharm.D., Ph.D. from No. IPR2024-01197
2012	<i>Reserved</i>
2013	M.E. Aulton (Ed.), Pharmaceutics: The Science of Dosage Form Design (2d. 2002)

2014	“Lozenge” Definition, Dennis B. Worthen (ed.), Dictionary of Pharmacy (2004)
2015	Paul J. Sheskey et al., Handbook of Pharmaceutical Excipients (8d. 2017)
2016	Hahm, H.A., Augsburger, L.L., Ch. 9 Orally Disintegrating Tablets and Related Tablet Formulations
2017	Ghosh, T.K. et al, Drug Delivery to the Oral Cavity Molecules to Market, Ch. 14 Quick dissolving oral dosage forms: Scientific and regulatory considerations from a clinical pharmacology and Biopharmaceutics Perspective (2005)
2018	Transcript of the August 25, 2025 deposition of Alan Parr, Pharm.D. from No. IPR2024-01197
2019	<i>Reserved</i>
2020	Cordova-Fraga T, Sosa M, Wiechers C, et al., Effects of anatomical position on esophageal transit time: a biomagnetic diagnostic tech-nique. World J Gastroenterol 14:5707–11 (2008)
2021	U.S. Patent No. 8,324,192
2022	Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, Patent and Exclusivity for: N213976, Product 001 Budesonide (Eohilia) Suspension 2mg/10ml, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=213976&Appl_type=N
2023	Memorandum from Director Coke Morgan Stewart to Members of the Patent Trial and Appeal Board re Enforcement and Non-Waiver of 37 C.F.R. § 42.104(B)(4) and Permissible Uses of General Knowledge in <i>Inter Partes</i> Reviews, dated July 31, 2025

I. INTRODUCTION

The challenged claims of U.S. Patent No. 9,486,407 (the “’407 patent”) relate to an orally disintegrating solid pharmaceutical composition¹ comprising a topical corticosteroid (i.e., a corticosteroid with no significant systemic glucocorticoid or mineralocorticoid activity) that disintegrates within 60 seconds or less according to the USP <701> Disintegration Test and a method of treating an inflammatory condition using said ODT. EX1001, 1:14-31, 5:7-16. As the claimed composition disintegrates within 60 seconds, it forms a suspension with the small amount of saliva produced during that timeframe. As the suspension is swallowed, a therapeutically effective amount of the corticosteroid is released and deposited in the esophagus. This allows the orally disintegrating solid pharmaceutical composition to treat an inflammatory condition of the upper gastrointestinal tract, such as eosinophilic esophagitis (“EoE”). EX1001, 1:14-31, 5:7-16.

Petitioner cannot established *prima facie* obviousness because the cited references do not motivate or provide a reasonable expectation of success in arriving at the claims of the ’407 patent. As discussed below, the prior art teaches the use of 8-12mL viscous liquids or slow dissolving lozenges (e.g., that produces 8-12mL

¹ The orally disintegrating solid pharmaceutical composition will be referred to as “ODT” herein.

liquid) to treat EoE. No reference recognizes that an ODT that disintegrates within 60 seconds can be used to topically deposit a topically acting corticosteroid on the upper gastrointestinal tract to treat EoE.

II. THE GROUNDS

The Board instituted review on all grounds outlined in the Petition. Paper 7, 11. In Grounds 1 and 3, Petitioner asserts that claims 1-4, 16-19, 21-23 and 35-39 would have been obvious over US 2007/0111978 (“Dohil”) and claims 5-15 and 20 would have been obvious over Dohil and US 2005/0232988 (“Venkatesh”). Petitioner argues that Dohil’s disclosure of a “lozenge or other similar tablet... [that] dissolve[s] rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus[,]” teaches the claimed ODT. Pet., 20. Petitioner cites to Venkatesh for teaching rapidly dispersing microgranules. Pet., 53-64. Dohil alone and in combination with Venkatesh do not teach the claimed invention.

Dohil’s lozenge or similar tablet is not an ODT that disintegrates within 60 seconds, and Dohil does not provide motivation or a reasonable expectation of success in arriving at the claimed ODT to treat EoE. Lozenges do not disintegrate in 60 seconds. A lozenge dissolves “slowly” over several minutes. EX2013, 413; *see also* EX2014, 201 (defining a lozenge as a “solid preparation...intended to dissolve or disintegrate *slowly*”) (emphasis added); EX2016, 293 (“Lozenges and buccal tablets are intended to dissolve *slowly* in the mouth, whereas, orally

disintegrating tablets must disperse or dissolve in the mouth quickly, within seconds.”) (emphasis added). Because Dohil describes its tablet as “similar” to a lozenge, Dohil’s “similar tablet” would also dissolve “slowly” over several minutes, like a lozenge. Dohil teaches a lozenge because dissolving slowly will produce the 8-12mL volume that Dohil teaches is required for “pan-esophageal mucosal coverage” and effective treatment of EoE. An ODT that dissolves within 60 seconds would not achieve this volume.

Venkatesh does not cure the deficiencies in Dohil, because Venkatesh does not teach or suggest an ODT that topically deposits a topically acting drug in the upper gastrointestinal tract (e.g., esophagus) for treating an inflammatory condition thereof (e.g., EoE). Venkatesh is directed generally to formulating orally disintegrating tablets containing rapidly dispersing microgranules and taste-masked microcapsules. Taste-masking, which refers to coating bitter-tasting drugs with certain polymers, shields the drugs from contacting the mouth and consequently the esophagus given the proximity to the mouth. EX2011², 89:1-18, 90:13-92:18, 93:12-16, 94:4-25; EX1020, [0027].

² The parties have agreed to make the deposition transcripts of *Dr. Falk Pharma GmbH v. Ellodi Pharma. L.P.*, IPR2024-01197, concerning U.S. Patent No. 8,771,729 (the “’729 patent”) of record in this matter. Petitioner’s expert’s

Petitioner uses a hindsight-driven analysis to presume that a person of ordinary skill in the art (POSA) would be seeking to formulate a tablet that disintegrates within 60 seconds or less based on the disclosure in Dohil. Petitioner provides no reasonable basis to establish a motivation to start from a tablet that disintegrates within 60 seconds, instead of Dohil's exemplified liquid formulation that was tested and shown to be effective. The general knowledge of a POSA cannot remedy this deficiency.³

In Grounds 2 and 4, Petitioner asserts that claims 1-4, 16-19, 21, 23-25 and 27-42 would have been obvious over WO 00/44351 ("Grother") and the FDA Guidance for Industry: Orally Disintegrating Tablets (2008) ("FDA Guidance"), and claims 5-15, 20 and 26 would be obvious over Grother, the FDA Guidance, and Venkatesh. Petitioner cites to Grother as teaching an ODT that can be used to

testimony regarding the '729 patent is equally relevant to his declaration here because the '407 patent is related to the '729 patent and Petitioner asserts the same art and arguments in both proceedings.

³ Pursuant to Director Stewart's July 31, 2025 Memorandum enforcing 37 C.F.R. § 42.104(B)(4), Petitioner improperly uses the "general knowledge" of a POSA to supply missing claim limitations. EX2023; *see, e.g.*, Pet., 23-26, 36-37, 40, 41, 43-46, 48-49, 50-52, 53-59, 62-68, 70-71.

administer a corticosteroid, the FDA Guidance for teaching disintegration with 30 seconds using the USP <701> Disintegration Test, and Venkatesh for rapidly dispersing microgranules. Pet., 34-53 (Ground 2), 64-71 (Ground 4). These references do not teach or suggest the claimed ODT and its use in treating EoE, because the combination of references fails to recognize that an ODT can be used to topically administer a corticosteroid to the esophagus.

Grother is not directed to any disease and does not teach ODTs designed to topically deposit a topical (non-systemically active) drug in the upper gastrointestinal tract for the treatment of inflammation of the upper gastrointestinal tract. Instead, Grother teaches a general “fast dispersing solid dosage form[]” platform that does not use gelatin and can be used with any active drug. EX1008, Abstract.

Similarly, the FDA Guidance is not directed to any particular disease, drug, or topical delivery of drugs to the upper gastrointestinal tract. It simply provides a definition for ODTs as disintegrating within 30 seconds as measured by the United States Pharmacopeia (USP) <701> Disintegration Test. EX1005, 2-3. It does not teach any ODT formulations or topical corticosteroids. Venkatesh does not cure the deficiencies because, as discussed above, Venkatesh’s taste-masking layer would prevent a corticosteroid from being deposited on the upper gastrointestinal tract.

Petitioner again relies purely on impermissible hindsight, and, as with Grounds 1 and 3, Petitioner offers no real reason why a POSA would have been motivated to formulate a solid pharmaceutical composition containing a topical corticosteroid that disintegrates in 60 second to topically deposit the corticosteroid on the upper gastrointestinal tract to treat inflammatory conditions thereof.

Because the Petition is factually and legally deficient, the Board should confirm the patentability of all challenged claims.

III. BACKGROUND

A. The '407 Patent (EX1001)

The '407 patent is directed to ODTs containing a topically active corticosteroid that topically administers a therapeutically effective amount of the corticosteroid to inflamed tissue of the upper gastrointestinal tract for the treatment of conditions associated with inflammation of the upper portion of the gastrointestinal tract. EX1001, 1:14-31, 5:19-24. Topically depositing a therapeutically effective amount of a topically acting corticosteroid to the upper gastrointestinal tract (e.g., esophagus) is challenging, due to the constant flow of saliva, peristalsis, and gravity pushing the corticosteroid down toward the stomach. EX2007, ¶ 45. Despite these challenges, Patent Owner developed the first ODT for topical treatment of EoE.

EoE is an inflammatory condition of the esophagus. EX1001, 1:26-28. Prior

treatments for EoE included corticosteroid formulations designed for inhalation that were instead applied to the back of the throat, (EX1001, 1:32-44), as well as oral administration of systemically active corticosteroids (EX1001, 1:45-53). These treatments posed undesirable side effects, including candidiasis infection and suppression of immune function, respectively. EX1001, 1:32-53.

The ODT and method of treatment claimed in the '407 patent solves these problems by formulating an ODT with a corticosteroid that has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration (i.e., a topically active corticosteroid). The ODT disintegrates within 60 seconds to form a solution or dispersion that is swallowed, and the topically active corticosteroid is released and topically deposits the corticosteroid on the upper gastrointestinal tract, including the esophagus. EX1001, 1:60-2:3. Disintegration of the tablet and dissolution (drug release) occur near simultaneously, resulting in drug deposition on the esophagus within 1-2 seconds of swallowing and before the disintegrated tablet passes to the stomach. EX2020, 5708 (“...liquid [esophageal transit time] lasts approximately 1 to 2 s...”). This mechanism of localized delivery mitigates the undesirable side effects of systemic corticosteroids used for treating EoE and candidiasis infections associated with oral corticosteroid administration. EX1001, 1:60-2:3, 4:1-5.

PO surprisingly discovered that the claimed ODT can deposit a

therapeutically effective amount of a topically acting corticosteroid on the esophagus in the short period of time (~1-2 seconds) it takes the suspension to transit the esophagus and effectively treat EoE (despite disintegrating significantly faster than Dohil's lozenge or similar tablet, and not coating the esophagus with 8-12mL, as taught by Dohil), and without causing candidiasis infections. EX2010; EX2020, 5708. It is surprising that the claimed pharmaceutical composition mitigates candidiasis since an orally disintegrating composition would remain in the oral cavity longer than Dohil's liquid formulation or the formulations mentioned in the background of the '407 patent that were designed for inhalation that are instead applied to the back of the throat. EX2003, 188; *see also* EX2010, 89.

IV. THE LEVEL OF ORDINARY SKILL IN THE ART

In this proceeding only, Patent Owner generally accepts Petitioner's proposed level of ordinary skill in the art.

V. CLAIM CONSTRUCTION

In this proceeding only, Patent Owner generally accepts Petitioner's proposed constructions.

VI. PETITIONER FOCUSES ON IRRELEVANT BACKGROUND PRIOR ART

In describing the state of the prior art, Petitioner focuses on irrelevant prior art disclosing budesonide and orally disintegrating pharmaceutical compositions, none of which is relied on in Petitioner's or its expert's obviousness analysis and

none of which teaches that an ODT can be used to topically administer a corticosteroid to the upper gastrointestinal tract to treat EoE. EX2004, 13:2-21; EX2011, 31:20-21, 41:1-15.

A. The Budesonide Prior Art Either Cannot Deposit Budesonide on the Upper Gastrointestinal Tract or uses Dohil's 8-12mL Liquid

Petitioner cites to various references, including Petitioner's product Budenofalk, as teaching the use of budesonide for treating inflammatory conditions such as Crohn's disease and ulcerative colitis. Pet., 5-6 (citing EX1025, EX1009, EX1010, EX1011, EX1012, EX1013, EX1026, EX1027, EX1028). These references all relate to the use of budesonide for treating inflammation of the lower gastrointestinal tract, and almost all of these prior art formulations use enterically coated budesonide tablets designed to deliver budesonide to the lower gastrointestinal tract. EX2007, ¶¶63-71. Because an enteric coating is designed to prevent drug release until the drug passes through the stomach to the intestines, enterically coated budesonide cannot be deposited in the upper gastrointestinal tract as required by the claims of the '407 patent. Petitioner does not rely on any of these background references in its obviousness analysis. EX2007, ¶¶63-76.

Petitioner goes on to cite Aceves et al. 2005 and 2007, which were included in Dohil's Examples. Pet., 6-7 (citing EX1014, 1015). As Petitioner points out, Aceves 2005 and 2007 reported successful treatment of EoE with 8-12mL of a

viscous **liquid** suspension of budesonide. Pet., 6 (citing EX1014, 706; EX1015, 1, 6, 8). The viscous liquid suspension of budesonide and its successful treatment in EoE are included in Dohil. *Id.* (citing EX1002). Petitioner does not rely on any of these background references in its obviousness analysis. EX2007, ¶¶ 72-76.

Petitioner cites to several references that highlight advantages of using ODTs. Pet., 7-9 (citing EX1019, 310-311; EX1018, 466-67; EX1017, 172). However, none of these references recognize that ODTs can be used to topically deposit a topically acting drug to the upper gastrointestinal tract. To the contrary, all prior art ODTs were used to facilitate easy administration of **systemically active** drugs **to the stomach and lower intestines**, and promoting systemic absorption. The Petition and Petitioner's expert failed to provide any evidence of ODT used for topical delivery of a topically active drug to the upper gastrointestinal tract. Remarkably, Petitioner's expert admits he was not aware of any such formulation in the prior art. EX2011, 18:5-8; *see also* EX2004, 10:19-25.

Petitioner further refers to a list of commercially available ODTs. Pet., 9-11. None of the compositions contain topically acting corticosteroids, or any other topically acting drug or were used to treat an inflammatory condition of the upper gastrointestinal tract or EoE. EX2007, ¶¶ 78-79.

VII. PETITIONER'S ANALYSIS OF THE PRIOR ART IS GUIDED BY IMPERMISSIBLE HINDSIGHT

Petitioner argues that ODT containing budesonide were known in the art, but this not true and based on impermissible hindsight. As discussed below, the art the Petitioner cites does not actually teach or suggest using an ODT that disintegrates within 60 seconds to topically administering a topically acting drug to the upper gastrointestinal tract (e.g., esophagus).

A. Dohil

Petitioner cites to Dohil for its disclosure of a “lozenge or other similar tablet” that *dissolves* rapidly in the mouth or esophagus as teaching an ODT. Pet., 11, 20; EX1002, [0032]. Petitioner only cites to three paragraphs in Dohil which generally refer to solid dosage forms. Pet., 6, 11, 20; EX2007, ¶¶ 81-82. However, Dohil does not exemplify or provide an enabling disclosure of a lozenge or other similar tablet, and is silent regarding the disintegration rate. In fact, Dohil does not even use the term disintegrate, as recited in the claims of the '407 patent. Dohil refers to dissolve, and dissolve and disintegrate are different processes. EX2018, 21:19-22. While Petitioner does not say dissolve and disintegrate are the same, PO assumes the Petition is equating the terms. The remaining disclosure in Dohil, which spans approximately 110 paragraphs, is exclusively related to liquid formulations of budesonide. This is because Dohil's invention is a liquid composition containing a

viscosity enhancing agent that improves contact of the corticosteroid with the esophagus that is “simple” and “palatable” and formulated with an 8-12mL volume that provides “pan-esophageal mucosal coverage” to effectively treat EoE. EX2011, 72:25-74:6, 61:3-9, 66:17-20, 68:10-12, 68:22-24, 70:8-12; EX1002, [0067].

To this end, Dohil teaches that it “is often difficult to deliver an effective dose of corticosteroid to the targeted area of the esophagus” and a liquid solution solves this problem. EX1002, [0007], [0009] (“A liquid, long-acting topical corticosteroid preparation is needed.”). Dohil teaches that its liquid compositions are formulated with a viscosity enhancer to deliver to the esophagus a viscous liquid containing budesonide that coats the esophagus. EX1002, [0011], [0013], [0021], [0038], [0042]-[0045], [0046], [0048]-[0070]. Dohil also teaches that 8-12mL of liquid is necessary to provide an effective amount of the corticosteroid to the esophagus. EX1002, [0031], [0053], [0067] (“[OVB] may have advantages over other therapies in that...its volume (8-12ml) provides pan-esophageal mucosal coverage...”).

All three examples in Dohil discuss an oral viscous liquid budesonide formulation (referred to as OVB). EX1002, [0056]-[0070]. The OVB liquid formulation is the only formulation made and tested in these examples, and the data shows that it effectively treats EoE in children. Dohil highlights several advantages of the OVB liquid formulation, including palatability and effective drug contact with the esophagus. EX1002, [0067] (“It may have advantages over other therapies in

that it is palatable, its volume (8-12ml) provides pan-esophageal mucosal coverage and it requires only once daily administration.”); *id.*, [0056]-[0070]. More specifically, in Examples 1 and 2, the patients were administered the viscous liquid formulation daily, and both patients showed improvement of EoE symptoms and complete resolution or normal appearing esophagus after treatment. EX1002, [0046]-[0047]. In Example 3, patients were given the viscous liquid formulation and 90% of patients showed improvement after treatment. EX1002, [0048], [0053], [0060]. Dohil does not mention any problems with the viscous liquid formulation. EX2007, ¶ 86. Thus, a POSA would understand Dohil as teaching that a specific, large volume (8-12mL) of a viscous liquid formulation is needed to treat EoE because it is capable of coating the esophagus and topically delivering an effective dose of a topical corticosteroid to the esophagus. EX1002, [0067]. Thus, Petitioner’s interpretation of Dohil as providing motivation to formulate the claimed orally disintegrating composition that disintegrates within 60 seconds is pure hindsight. EX2007, ¶ 86-87.

Petitioner points to the fact that Dohil describes its lozenge or similar tablet as dissolving rapidly, as teaching the claimed ODT. Pet., 19-30. This is incorrect for several reasons. While Dohil mentions that the “lozenge or other similar tablet...dissolve[s] rapidly,” this does not lead a POSA to an ODT that disintegrates in 60 seconds. Lozenges are well known in the art to dissolve *slowly*. EX2013, 413;

see also EX2014, 201 (defining a lozenge as a “solid preparation...intended to dissolve or disintegrate ***slowly***”) (emphasis added). The art also distinguishes lozenges from other ODTs. EX2016, 293 (“Despite a surge of orally disintegrating tablets in the market in the recent years, they potentially can be confused with other solid oral dosage forms that are consumed without additional water intake, including ***lozenges***, buccal tablets, and chewable tablets. Lozenges and buccal tablets are intended to dissolve ***slowly*** in the mouth, whereas, orally disintegrating tablets must disperse or dissolve in the mouth quickly, within seconds.”) (emphasis added); EX2017, 341 (distinguishing quick/fast/rapid/mouth-dissolving tablets and fast/quick-melting tablets from lozenges). Indeed, Petitioner’s expert also admits that a typical lozenge dissolves slowly. EX2011, 62:13-15. Because lozenges dissolve slowly over several minutes, Dohil’s similar tablet would also dissolve over several minutes, just like a lozenge.

Dohil’s reference to “dissolve rapidly” is also consistent with a POSA’s understanding of the mechanism of drug release from a lozenge, and does not indicate an ODT disintegration within 60 seconds. Lozenges provide an initial rapid release of drug when the lozenge contacts saliva and then continue to dissolve slowly over several minutes, continuing to release drug. The process of dissolving slowly over a several minutes would provide the 8-12mL volume of viscous liquid that Dohil teaches is required to coat the esophagus and treat EoE. EX1002, [0067] (“It

may have advantages over other therapies in that it is palatable, its volume (8-12ml) provides pan-esophageal mucosal coverage and it requires only once daily administration.”); EX2007, ¶¶ 73-74. This is reinforced by Dohil’s teaching to dissolve a lozenge in 8-12mL to treat EoE (“for children or other patients that may have difficulty with a dissolving lozenge, the lozenge may be ground or otherwise dissolved...reaching a total volume presented in embodiments herein[,]” i.e. 8-12mL. EX1002, [0032], [0067]). Interpreting Dohil to teach disintegration within 60 seconds reads into Dohil a disclosure that simply is not there. Petitioner starts with the claim language of the ’407 patent and attempts to force Dohil’s disclosure to fit into the claims of the ’407 patent.

B. Grother

Petitioner also cites to Grother as disclosing an ODT containing budesonide. Pet., 11 (citing EX1008). Petitioner’s reliance on Grother is based purely on impermissible hindsight because, as confirmed by Petitioner’s expert, Grother is not directed to any particular disease and does not teach topical deposition of a topically active drug to the upper gastrointestinal tract (e.g., esophagus). EX2011, 75:5-10, 79:1-10.

Instead, Grother is directed to a new fast dispersing tablet platform for any drug that is “essentially free or absolutely free of mammalian gelatin.” EX1008, Abstract. To this end, Grother describes the issues with using gelatin in formulating

fast dispersing dosage forms, such as increased processing times, increased costs, and lack of homogeneity. EX1008, 2-3. Grother describes its invention as eliminating gelatin from the formulations and using modified starches instead, listing the various advantages of modified starches, such as improved stability and strength of the dosage form, allowing the use of sweeteners to improve taste, and elimination of exposure to undesirable agents. EX1008, 3-6; *see also* EX2007, ¶ 94.

Grother discloses that “[a]ny drug may be used as the active ingredient in the composition of the present invention.” EX1008, 15:19-20. Grother then goes on to list hundreds of drugs in multiple drug classes across six pages. EX1008, 16-21; EX2007, ¶ 95. Six of the eight examples disclosed in Grother do not even include a drug. EX1008, 22-31. Examples 7 and 8 include three drugs, none of which are topically acting corticosteroids. EX1008, 29, 31. A POSA would therefore understand Grother to disclose a general platform technology, for which any drug may be used, not ODTs containing topical corticosteroids for the treatment of EoE. EX2007, ¶ 96. Thus, Petitioner’s arbitrary selection of budesonide and fluticasone is pure hindsight based on Patent Owner’s claims.

Petitioner arbitrarily cites to Grother’s disclosure of corticosteroids, specifically fluticasone and budesonide, but does not acknowledge that Grother does not distinguish between topically acting and systemically acting drugs in the plethora of drugs it lists. Pet., 11, 36; EX1008, 18:15-18; EX2011, 78:4-8. Indeed,

fluticasone and budesonide are listed among systemically acting corticosteroids, which are expressly excluded from the scope of the '407 patent's claims, including hydrocortisone, prednisone, prednisolone, methylprednisolone, dexamethasone and betamethasone. *Compare* EX1001, 3:30-33, *with* EX1008, 18:15-19. The other drugs and drug classes disclosed in Grother are also predominantly systemically active drugs. Moreover, Petitioner remarks that one of the advantages of ODTs is the ability of the active ingredient to be absorbed through the mucosa of the gastrointestinal tract, beginning in the mouth. Pet., 2, 7, 9. A POSA would therefore be motivated to select a systemically acting drug from Grother's list of drugs for this benefit rather than a topically acting corticosteroid. This is because topically acting corticosteroids, such as fluticasone and budesonide, provide therapeutic effects from topical contact, not absorption. On the other hand, systemically acting drugs must be absorbed. As explained in further detail below, Petitioner does not explain why a POSA would be motivated to look to Grother when looking to formulate treatments for inflammatory conditions of the upper gastrointestinal tract or EoE. Petitioner instead begins with the premise that a POSA would seek to formulate an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet without providing any reasoning as to why a POSA would want to make an orally disintegrating composition for treatment of EoE at all.

C. Singh and Cherukuri

Finally, Petitioner cites to Singh and Cherukuri for disclosing ODTs containing budesonide. Pet., 11-12 (citing EX1035, EX1036). Petitioner does not rely on either reference as a ground for obviousness. Like Grother, Singh and Cherukuri list numerous classes and types of drugs, and neither Singh nor Cherukuri distinguishes between topical or systemic drugs in their laundry list of drug. Nor does either reference discuss using an ODT to topically deposit a topically active drug on the upper gastrointestinal tract (e.g., esophagus), or how to effectively treat inflammation of the upper gastrointestinal tract. Thus, a POSA would understand Singh and Cherukuri to be directed towards general ODT platforms, and Petitioner's arbitrary selection of budesonide is pure hindsight based on Patent Owner's claims. EX2007, ¶ 98.

D. FDA Guidance

Petitioner relies on the FDA Guidance for Grounds 2 and 4 and as general background on ODTs. Pet., 12-13. Petitioner's expert admitted that the FDA Guidance simply provides a definition for ODTs and is not directed to formulations for treating inflammation of the upper gastrointestinal tract. EX2011, 56:15-21; *see also* EX2007, ¶ 93. Specifically, the FDA Guidance states that ODTs are defined as “[a] solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.” EX1005, 2. The

FDA Guidance goes on to state that ODTs disintegrate within “approximately 30 seconds or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative[.]” EX1005, 2. The FDA Guidance does not discuss or even recognize that an ODT can be used to topically administer a topically acting drug to the esophagus. Thus, Petitioner’s reliance on the FDA Guidance is driven by pure hindsight as it has no relevance to the problems solved by the ’407 patent, namely topically depositing a corticosteroid on the upper gastrointestinal tract to treat inflammatory conditions thereof, such as EoE.

E. Starting with an ODT when Solving the Problem of Delivering Topically Acting Corticosteroid to Upper Gastrointestinal Tract is Impermissible Hindsight

Petitioner does not analyze the art as a POSA, because Petitioner is not focused on finding a treatment for EoE. Petitioner starts with the presumption that a POSA would be motivation to formulate ODT that disintegrates within 60 seconds as measured with the USP <701> Disintegration Test. This is evident from Petitioner’s reliance on ODTs used to administer systemic drugs to the gut. Pet., 7-11. Perhaps the most striking evidence of Petitioner’s hindsight-driven analysis is its expert’s admission that it was not aware of and conducted no specific search for any prior art orally disintegrating composition used to deliver a topically acting drug to the esophagus. EX2011, 18:5-13 (“Q[:] Are you aware of any drugs that have been developed as an ODT for topical administration of the esophagus? A[:] No, I

do not...Q[:] You didn't do any investigation into that for this declaration, correct?

A[:] No, ma'am"); EX2004, 10:19-25 (testifying that Petitioner's expert submitted his declaration in this proceeding prior to being deposed in *Dr. Falk Pharma GMBH v. Ellodi Pharma. L.P.*, IPR2024-01197). This is the epitome of hindsight. "The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time." *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed. Cir. 1985).

In contrast to the Petition, a POSA trying to treat inflammation of the upper gastrointestinal tract would have begun by first identifying formulations that were effective for treating inflammation of the upper gastrointestinal tract. Out all of the references cited in the Grounds, only Dohil discusses treatments for EoE. From the disclosure in Dohil and the "off-label" treatments addressed in the '407 patent, a POSA would understand that liquid and inhaled formulations were known to deliver an effective amount of a corticosteroid to the upper gastrointestinal tract. EX1002, [0006], [0046]-[0070]; EX1001, 1:32-53. Further, from Dohil, a POSA would understand that 8-12mL of viscous liquid provides pan-esophageal coverage and increases the duration of contact of the topical corticosteroid with the inflamed esophagus to effectively treat EoE. EX1002, [0031], [0053], [0067]. These formulations are a logical starting point because the delivery mechanism ensures contact of topically active budesonide with the esophagus, whereas as Petitioner's

evidence shows that prior to the '407 patent ODTs had only been used to administer systemically active drugs to the stomach for adsorption.

Thus, a POSA would start with Dohil's liquid. A POSA would have no motivation to fundamentally change Dohil's liquid composition and formulate budesonide as a solid composition. In fact, Dohil teaches that solid formulations will not be as effective as the 8-12mL viscous liquid. "[OVB] may have advantages over other therapies in that...its volume (8-12ml) provides pan-esophageal mucosal coverage...." EX1002, [0067]. Because Dohil refers to a "lozenge or other similar tablet" and then states that OVB is superior to other therapies, a POSA would understand Dohil as teaching that OVB is superior to a lozenge or similar tablet. EX1002, [0032], [0067].

Assuming a POSA would formulate budesonide as a solid composition, it would not be an ODT that disintegrates within 60 seconds as claimed in the '407 patent. Based on Dohil's teaching that a large volume of viscous liquid (8-12mL) is necessary for pan-esophageal coating and efficacy, a POSA would therefore be motivated to provide longer disintegration times to increase volume and coating of the esophagus, such as with Dohil's lozenge which would dissolve over several minutes. A lozenge (or similar tablet) that dissolves slowly, over several minutes, would produce Dohil's 8-12mL volume. EX2005, 303 (the rate of saliva "increases to about 4[.]0-5[.]0 ml / min during eating, chewing and other stimulating

activities.”). This is consistent with the art-recognized definition of a lozenge. EX2013, 413; EX2014, 201; EX2016, 293. ODTs that disintegrate within 60 seconds would not produce Dohil’s 8-12mL and would therefore be counterintuitive.

VIII. THE EPO DECISION DOES NOT CONTROL

Petitioner argues that because the EPO found different claims of a European counterpart to the ’407 patent obvious over Dohil, so too should the Board. Pet., 13-16. EPO proceedings, however, follow a different process according to different rules and are not binding on U.S. tribunals. Contrary to Petitioner’s assertion, the EPO found that the disintegration time of 60 seconds was a “distinguishing” feature over Dohil. EX1004, ¶ 36.4. A “technical effect,” however, could not be derived from the examples in the European patent application. EX1004, ¶¶ 36.5, 36.6. According to the EPO, this was because the example related only to fluticasone while the claims were directed to budesonide. EX1004, ¶ 36.6.

The “technical effect” is an EPO requirement to establish inventive step. There is no such requirement under U.S. patent law for establishing non-obviousness. In the U.S., non-obviousness can be based on lack of motivation or reasonable expectation of success. Further, post-filing data can be used as evidence of efficacy and unexpected results. *Knoll Pharm. Co. v. Teva Pharms. USA, Inc.*, 367 F.3d 1381, 1385 (Fed. Cir. 2004) (“There is no requirement that an invention’s properties and advantages were fully known before the patent application was filed

... [n]or is it improper to conduct additional experiments and provide later-obtained data in support of patent validity.”). To that end, submitted herewith is evidence showing that a budesonide ODT can achieve equivalent efficacy as Dohil’s liquid budesonide formulation at half the dose and produces fewer side effects. EX2006. As such, Petitioner’s reliance on the EPO decision is irrelevant to the proceeding at hand. U.S. courts and the Board routinely reject the relevance of such decisions. *See, e.g., Medtronic, Inc. v. Daig Corp.*, 789 F.2d 903, 907-08 (Fed. Cir. 1986) (refusing to adopt an obviousness holding of a German tribunal regarding a German counterpart patent because “[t]he patent laws of the United States are the laws governing a determination of obviousness/nonobviousness of a United States patent”); *Smith & Nephew, Inc. v. ConvaTec Techs. Inc.*, IPR2013-00097, Paper 76 at 3 (P.T.A.B. Feb. 24, 2014) (declining to enter into the record a European Patent Office decision regarding a European counterpart to a challenged U.S. patent, explaining that “the [EPO] decision does not involve the U.S. patents at issue in these proceedings, is not based on U.S. law, and is thus of limited relevance to the instant proceedings”).

IX. THE CLAIMS OF THE '407 PATENT ARE PATENTABLE**A. It was Not Obvious to Formulate ODT to Topically Deposit a Corticosteroid on the Upper Gastrointestinal Tract and treat EoE**

In Grounds 1 and 3, Petitioner relies on Dohil and Venkatesh to challenge claims 1-4, 16-19, 21-23, 35-39, and 5-15, 20, respectively. As discussed in more detail below, a POSA had no motivation to modify Dohil and formulate the claimed ODT. This is because Dohil teaches a lozenge, which is known in the art to dissolve “slowly” and would produce the 8-12mL of viscous liquid needed to provide pan-esophageal coverage and effectively treat EoE. EX1002, [0067]. Venkatesh does not cure these deficiencies because Venkatesh’s particles are coated with a water-insoluble or pH-responsive polymer for the purpose of taste-masking, and the taste-mask coating would prevent the corticosteroid from being topically deposited on the upper gastrointestinal tract. EX1020, [0009], [0018], [0022], [0027]; EX2007, ¶¶ 104-110, 139-143. Thus, Petitioner’s Grounds 1 and 3 fails and claims 1-23 and 35-39 are patentable.

1. Dohil Does Not Suggest or Teach ODTs as Required by Claims 1-4, 16-19, 21-23, and 35-39

Petitioner argues that Dohil discloses an ODT comprising a corticosteroid that disintegrates within 60 seconds. Pet., 20-29. Petitioner points to Dohil’s disclosure of “a lozenge or other similar tablet” that “wo[u]ld dissolve rapidly in the mouth or esophagus[.]” Pet., 20-21 (citing EX1002, [0032]). Petitioner goes on to argue that

“[i]t would have been obvious to formulate Dohil’s rapidly dissolving lozenge or tablet to disintegrate within 60 seconds” using the USP <701> Disintegration Test based on the FDA Guidance. Pet., 24. According to Petitioner, “[a] POSA seeking to formulate budesonide into an orally disintegrating pharmaceutical composition would be highly motivated to follow the FDA Guidance that such a composition should disintegrate within 30 seconds or less when tested using the USP <701> Disintegration Test.” Pet., 25. This argument presumes that a POSA would be motivated to make an ODT based on the disclosure in Dohil, which is not true.

As explained above, Dohil’s invention is an 8-12mL viscous liquid budesonide formulation (referred to in Dohil as OVB) that provides pan-esophageal coverage and effectively treats EoE, and all three examples administer the viscous liquid formulation and treat EoE. EX1002, [0013], [0030], [0031], [0036]-[0070]. Dohil does not disclose any examples using a solid dosage form. Thus, Dohil teaches that a viscous liquid budesonide suspension is successful in treating EoE. EX2007, ¶¶ 84-86, 105-106.

Dohil never mentions a solid dosage form that disintegrates within 60 seconds. Dohil discloses solid compositions in only two paragraphs, as a “dissolving tablet”/“dissolving wafer” and “lozenge or other similar tablet.” EX1002, [0013], [0032]. A POSA would understand the first disclosure of dissolving tablets or wafers to refer to solid forms that are dissolved in water before oral administration

and not tablets that disintegrate in the mouth, as solid dosage forms that are dissolved in water before oral administration were well known at the time. *See* EX1017, 181; EX2007, ¶ 82, 107.

Regarding the second disclosure of a lozenge or similar tablet, this does not refer to an ODT that disintegrates in 60 seconds for several reasons. First, Dohil does not call its lozenge or other similar tablet an ODT, even though ODTs were known in the art, or explicitly state that the lozenge or other similar tablet dissolves within 60 seconds. EX1002, [0032]. While Petitioner cites several synonyms for ODTs, nowhere does Petitioner assert that lozenges are synonymous with ODTs. Pet., 7. Thus, Dohil also does not act as its own lexicographer to change the definition of its lozenge to mean an ODT. Second, lozenges are known in the art to dissolve over several minutes, and therefore a “similar tablet” would also dissolve over several minutes. EX2013, 413; EX2014, 201; EX2016, 293 (“Lozenges and buccal tablets are intended to dissolve slowly in the mouth, whereas, orally disintegrating tablets must disperse or dissolve in the mouth quickly, within seconds.”). The use of the phrase “dissolve rapidly” does not change the well-understood definition of a lozenge. As Petitioner’s expert has admitted, “dissolve” refers to drug release. EX2018, 21:19-22. Thus, Dohil is merely describing the initial release of drug from the lozenge which may occur rapidly after oral administration, but lozenges – by definition – dissolve completely over several

minutes. EX2013, 413; EX2014, 201; EX2016, 293; EX2017, 341. Third, “dissolv[ing] slowly” is necessary to achieve the 8-12mL volume of liquid that Dohil teaches provides pan-esophageal coverage and is necessary for effective treatment of EoE. Consequently, the disclosure of a lozenge and similar tablet cannot be a disclosure of an orally dissolving composition that disintegrates in 60 seconds as claimed.

Lastly, Dohil acknowledges that its lozenge is not easily swallowed, so it is not an ODT, which the Petition acknowledges, are specifically designed for *easy swallowing*. Pet., 8. However, Dohil provides alternative administration instructions: “for children or other patients that may have *difficulty with a dissolving lozenge*, the lozenge may be ground or otherwise dissolved...reaching a total volume presented in the embodiments herein” i.e., 8-12mL. EX1002, [0032] (emphasis added). If, as Petitioner contends, a lozenge is an ODT, then these same patients, for the same reasons, could not use an ODT formulation. Nonetheless, this disclosure confirms Dohil’s lozenge *is not* an ODT that would rapidly disintegrate because if it were, the lozenge would not need to be “ground up” or dissolved in 8-12ml of a liquid which is then swallowed to treat EoE. EX1002, [0032], [0067]; EX2007, ¶ 108.

Petitioner also argues that a lozenge can be formulated with a disintegrating agent. Pet., 53-54. Petitioner’s own reference, Danckwerts (EX1017), expressly

contradicts this argument. Danckwerts teaches that lozenges are manufactured “*without disintegrants* and are intended to be sucked by patients.” EX1017, 181 (emphasis added); *see also* EX2013, 413 (“Disintegrants are not used in the formulation...”). As acknowledged by Petitioner’s expert, the mere reference to a disintegrant does not teach or suggest an orally disintegrating composition because conventional (non-orally disintegrating) tablets include disintegrants. EX2011, 65:2-11.

Thus, Dohil does not teach or suggest a solid orally disintegrating pharmaceutical composition that disintegrates within 60 seconds for at least the reasons stated above.

2. Dohil Provides No Motivation to Formulate an ODT

Petitioner asserts that “[i]t was desirable for the disintegration time of rapidly dissolving solid compositions to vary ‘from several seconds to about a minute’” and that it would have been obvious to formulate Dohil’s lozenge or similar tablet to disintegrate within 60 seconds in view of the FDA Guidance. Pet., 24 (citing EX1018, 434).

However, as discussed above in Section VII.A, Dohil’s invention is a liquid formulation that is palatable and simple, and, most importantly, effective for treating EoE. The Petition fails to identify any issue with Dohil’s viscous liquid formulation that would motivate a POSA to fundamentally change dosage forms to an ODT. To

the contrary, Dohil's viscous liquid has several benefits, namely palatability, the ability to provide pan-esophageal coverage, and efficacy. EX2007, ¶ 113. Further, as Petitioner's expert admitted in his deposition testimony, Dohil does not disclose any issues with dosing, compliance or stability with its OVB, and the data disclosed in Dohil shows that OVB is effective in treating EoE. EX2011, 72:25-74:6. Without a recognized problem, a POSA had no motivation to change Dohil's effective liquid dosage form to an ODT. EX2007, ¶¶ 113. It is only through impermissible hindsight, guided by the teachings of the '407 patent, that a POSA would disregard Dohil's effective liquid formulation, and formulate an ODT that disintegrates within 60 seconds based on Dohil. EX2007, ¶¶ 111-116. "The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time." *Interconnect Planning Corp.*, 774 F.2d at 1138. An obviousness combination is only legitimate if the petition provides an "explanation as to how or why the references would be combined to arrive at the claimed invention," failing which "we are left with only hindsight bias that *KSR* warns against." *Metalcraft of Mayville, Inc. v. The Toro Co.*, 848 F.3d 1358, 1367 (Fed. Cir. 2017). Petitioner and its expert fail to provide such an explanation, instead jumping to the conclusion that a POSA would seek to formulate budesonide in an ODT that disintegrates within 60 seconds based on the passing references of a lozenge in Dohil.

An ODT is significantly more complicated and expensive to manufacture than Dohil's liquid and there is no evidence in the prior art that an ODT had been used to topically deposit a topically active drug to the upper gastrointestinal tract. EX2007, ¶¶ 113. *In re Cyclobenzaprine*, 676 F.3d 1063, 1068-69 (Fed. Cir. 2012) (holding that a petition must demonstrate "that a skilled artisan would have had reason to combine the teaching of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success from doing so.") (citation omitted).

To fabricate a motivation, Petitioner's expert characterizes Dohil's examples as a "proof of concept study" or "pilot studies" and stated that Dohil was using a simple formulation to determine if budesonide worked for EoE. EX2011, 61:3-62:3. But this statement is illogical and inconsistent with the background literature Petitioner's expert cited to show that budesonide was known to be effective in treating EoE. EX2011, 61:3-62:3. As explained in the '407 patent and Dohil, budesonide was already known to be effective in treating EoE. EX1001, 1:32-44, 3:30-33; EX1002, [0067]; *see also* EX1014 (showing budesonide has previously been used to treat EoE), EX1015 (same). Thus, Dohil already invented an improved formulation, an 8-12mL viscous solution, and showed that it was effective for EoE.

Petitioner's position appears to be that liquid formulations are not commercially viable and a POSA would always change to a solid dosage form. *See*

EX2011, 72:9-73:25. This is incorrect. There were many commercially acceptable liquid formulations on the market and a POSA would have been able to take Dohil's "proof of concept" formulation and make a commercially viable liquid formulation for Dohil's larger clinical study. EX2027, 99:2-101:25, 104:24-106:25. In fact, that is exactly what happened. Dohil's "proof of concept" formulation was developed as "Eohilia," a liquid budesonide composition for treating EoE sold by Takeda Pharmaceuticals, Inc. Dohil was issued as U.S. Patent No. 8,324,192 (EX2021) which is listed in the Orange Book for Eohilia. EX2022.

Petitioner ignores Dohil's liquid formulation and focuses on Dohil's mention of a lozenge. As discussed above, lozenges are not ODTs because lozenges dissolve "slowly" to continuously release a drug (EX2013, 413; EX2014, 201; EX2016, 293; EX2017, 341). Petitioner and its expert fail to explain why a POSA would be motivated to modify a lozenge or similar tablet to disintegrate within 30 seconds using the USP <701> Disintegration Test as disclosed in the FDA Guidance. Modifying a lozenge to disintegrate within 30 seconds based on the FDA Guidance would render the lozenge and similar tablet unsatisfactory for its intended purpose or change the principal operation, because it would no longer dissolve slowly to continuously deliver the corticosteroid to the esophagus over several minutes as the lozenge dissolves. EX2007, ¶¶ 114-116; *see* MPEP § 2143.01 (V) ("If a proposed modification would render the prior art invention being modified unsatisfactory for

its intended purpose, there may be no suggestion or motivation to make the proposed modification”) (citing *In re Gordon*, 733 F.2d 900, 221, USPQ 1125 (Fed. Cir. 1984)); *see also* MPEP § 2143.01 (VI) (“If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.”) (citing *In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (C.C.P.A. 1959)).

Further, an ODT that disintegrates within 60 seconds would not produce 8-12mL of liquid and would not be expected to provide pan-esophageal coverage discussed in Dohil, and thus a POSA would not be motivated to pursue an ODT. EX1002, [0067]. In a related proceeding, *Dr. Falk Pharma GMBH v. Ellodi Pharma., L.P.*, IPR2024-01197, Petitioner’s expert testified that an ODT that disintegrates within 60 seconds would only produce about 1-2mL of liquid. EX2011, 50:17-24. Petitioner’s expert then back tracked and argued that a lozenge would generate 4-5mL per minute and could be effective to treat EoE. *Dr. Falk Pharma GmbH v. Ellodi Pharms., L.P.*, IPR2024-01197, Paper 20 at 10-11 (P.T.A.B July 14, 2025); EX2005, 303-304. Petitioner’s expert provided no support for this argument. Nonetheless, this is not the 8-12mL volume that Dohil teaches is required for efficacy. EX1002, [0067]. Put differently, an ODT that disintegrates within 60 or 30 seconds would not produce Dohil’s 8-12mL of liquid that provides pan-

esophageal coverage. A POSA therefore would not be motivated to modify Dohil to formulate an ODT that disintegrates within 60 or 30 seconds. Instead, a POSA would have been motivated to have longer disintegration times to produce 8-12mL and provide pan-esophageal coverage. *See DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1326 (Fed. Cir. 2009) (“An inference of nonobviousness is especially strong where the prior art’s teachings undermine the very reason being proffered as to why a person of ordinary skill would have combined the known elements[,]” i.e., where a prior art reference “teaches away” from the proposed modification) (citation omitted); EX2007, ¶¶ 114-118.

a. Venkatesh Does Not Cure the Deficiencies in Dohil

Petitioner asserts in Ground 3 that claims 5-15, 20 are unpatentable over Dohil and Venkatesh. A POSA also would not have been motivated to combine Venkatesh with the formulation in Dohil, because Venkatesh’s taste-masking prevents the drug from contacting the mouth and esophagus, whereas Dohil is directed to increase the contact of corticosteroids with the esophagus to treat EoE. Petitioner continues to rely on impermissible hindsight.

Venkatesh is not directed to topically acting corticosteroids, treatment of inflammation of the upper gastrointestinal tract, or topical delivery of drugs to the upper gastrointestinal tract. Instead, Venkatesh is directed generally to taste-masking of bitter drug particles administered using an ODT, as confirmed by

Petitioner's expert. EX2011, 90:13-92:18, 93:12-16, 94:4-25; EX1020, [0013]. Taste-masking involves coating with a drug with a water-insoluble polymer like ethylcellulose to prevent the drug from being released in saliva and contacting the oral cavity. EX1020, [0009], [0018], [0022], [0027]. Venkatesh also discloses cellulose acetate phthalate and hydroxypropyl methylcellulose phthalate as suitable polymers for taste-masking, which are pH-responsive polymers used for enterically coating drugs, so the drug is released after it passes through the stomach. EX1020, [0027]; EX2015, 191, 476. Thus, Venkatesh's taste-masking would prevent the bitter drug from topically contacting the oral cavity and, because of the proximity of the esophagus to the oral cavity, taste-masking would also prevent the drug from contacting the esophagus. Consequently, Venkatesh's taste-masking would not deposit a therapeutically effective amount of corticosteroid on the esophagus to treat inflammation of the upper gastrointestinal tract.

The claimed ODT disintegrates within 60 or 30 seconds. The transit time of the disintegrated ODT in the esophagus is 1 to 2 seconds. EX2020 (transit time for liquids in the esophagus is usually between 1 to 2 seconds). It is scientifically unreasonable to assume that, after 1 minute, all the taste-masked drug is released in a single burst over 1-2 seconds that the disintegrated ODT is present in the esophagus. A POSA would therefore not even consider Venkatesh to be relevant to the claims of the '407 patent. EX2007, ¶¶ 139-143.

Neither Petitioner nor its expert explain why a POSA would be motivated to look to Venkatesh. Instead, Petitioner merely states that a POSA would have been motivated to manufacture Dohil's lozenges according to Venkatesh. Pet., 53-64. Petitioner is wrong. A POSA developing a formulation to deposit a corticosteroid to the esophagus would have no motivation to combine Dohil and Venkatesh, because the combination would undermine Dohil's intended purpose of administering a corticosteroid to the esophagus (taste-masking would prevent a corticosteroid from contacting the esophagus). EX2007, ¶¶ 114-118, 145-148. A POSA would not remove Venkatesh's taste-masking because this would undermine Venkatesh's intended purpose of preventing contact of bitter or poor tasting drugs with the mouth. "A proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose." *In re Fritch*, 972 F.2d 1260, 1265 n.12 (Fed. Cir. 1992); *see also In re Ratti*, 270 F.2d at 813 (rejecting "suggested combination of references" that "would require ... a change in the basic principles under which the [primary reference] was designed to operate."); *Plas-Pak Indus., Inc. v. Sulzer Mixpac AG*, 600 F. App'x 755, 758-760 (Fed. Cir. 2015) (nonprecedential) (affirming the Board's decision in finding certain claims not unpatentable over obviousness as petitioner's contention that a first reference rendered the claims obvious fundamentally altered the operating principle of the prior art). Because Petitioner's

arguments regarding the alleged motivation to combine Dohil with Venkatesh are conclusory and do not explain any benefit to combining the references, they must be rejected. *See In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (declaring that “a petitioner cannot employ mere conclusory statements”); EX2007, ¶¶ 114-118, 145-148.

b. No Expectation of Success in Arriving at the Claimed Invention

Petitioner conclusively asserts that a POSA would have had a reasonable expectation of success formulating ODT that disintegrates within 60 seconds or 30 seconds and topically deposits the corticosteroid on the upper gastrointestinal tract (e.g., esophagus) based on Dohil and Petitioner’s allegation that formulating such compositions would have been routine at the time of the ’407 patent. Pet., 25-26.

Prior to the ’407 patent, an ODT had never been used to deposit a topically acting drug with no significant systemic activity on the upper gastrointestinal tract (e.g., esophagus) to treat a disease of the upper gastrointestinal tract. Indeed, Petitioner’s expert was not able to identify a single prior art ODT containing a topically acting drug that deposited the drug topically on the upper gastrointestinal tract. EX2011, 17:8-15. What has never been done cannot be routine.

Further, as explained above, Dohil teaches that 8-12mL of a viscous liquid is needed to provide pan-esophageal coverage and effectively treat EoE. EX1002,

[0067]. Unlike Dohil's liquid formulation, which is swallowed as an 8-12mL bolus dose, a POSA would know that when an ODT is administered orally, it disintegrates in the small volume of saliva produced in that short period of time and is swallowed. A POSA could not predict based on Dohil's disclosure whether the resulting volume or viscosity of the dissolved tablet would provide pan-esophageal coverage and effectively treat EoE. EX2007, ¶ 119, 146. Nothing in Dohil suggests that an ODT that disintegrates within 60 seconds would topically administer the corticosteroid to the upper gastrointestinal tract and effectively treat EoE. EX2007, ¶ 119. On the other hand, as explained above, because Dohil's lozenge or similar tablet dissolves slowly over several minutes, it would produce Dohil's efficacious 8-12mL liquid.

Petitioner's assertion for reasonable expectation of success in combination with Venkatesh fares even worse. Petitioner's only argument is that Venkatesh discloses successfully manufacturing orally disintegration compositions and so a POSA would have had a reasonable expectation of success in formulating the claimed ODT. Pet., 63-64. Petitioner fails to address the fact that Venkatesh is directed to taste-masking of bitter drug particles in ODTs in general, which prevents the drug from contacting the oral cavity. EX1020, [0002], [0009], [0013]-[0015], [0018]; *see also* EX2011, 90:13-92:18, 93:12-16, 94:4-25. Venkatesh's taste-masking also prevents topical administration of the active ingredient on the upper gastrointestinal tract. EX2007, ¶¶ 147-148. Petitioner fails to address Venkatesh's

taste-masking, much less articulate a reasonable expectation to remove this essential feature from Venkatesh's composition and still achieving a pleasant tasting formulation.

c. Dohil Does Not Disclose the Claimed Doses in the Context of a Tablet (Claims 1[ii], 35[i], 33-34)

Dohil also does not disclose the specific dose ranges required by claims 1 and 1[ii], 35[i], and 33-34. Liquid compositions and solid compositions differ in composition and delivery mechanism (Dohil's 8-12mL that provides pan-esophageal coating vs. the claimed ODT that disintegrates in a much smaller volume of saliva) and therefore require different considerations when determining the proper dose of an active drug. Petitioner cites to Dohil's disclosure of the doses administered to patients in Examples 1-3. Pet., 21. But the patients in Examples 1-3 were given the viscous liquid formulation. Dohil does not explain and Petitioner does not address the difference in formulation or the fact that doses for liquid compositions are not necessarily the same as a solid compositions. Indeed, Petitioner cited no evidence that the dosage of a topical acting drug in a liquid formulation is always the same as the dose of the same drug used in an ODT. Dohil therefore does not disclose any dose for an ODT based on its liquid compositions or teach a POSA how to extrapolate from a liquid to a solid. EX2007, ¶¶ 120-121. In fact, the art cannot teach this because the '407 patent is the first example of an ODT

topically administering a topically acting drug to the esophagus.

Petitioner fails to address a reasonable expectation of success of formulating an orally dispersing tablet with the claimed doses.

a. Dohil Does Not Teach or Suggest the Claimed Methods for Treatment (Claims 1-4, 16-19, 21-23)

Similarly, Dohil does not teach or suggest the method recited in claims 1-4, 16-19, and 21-23 of the '407 patent. As discussed above, Dohil does not teach or suggest an ODT that disintegrates within 60 seconds and therefore cannot disclose a method of treating inflammation of the upper gastrointestinal tract recited in claims 1-4, 16-19, and 21-23.

There would also be no reasonable expectation of success in treating the inflammation of the upper gastrointestinal tract recited in claims 1-4, 16-19, and 21-23 by administering an ODT that disintegrates within 60 seconds as claimed, because there is no reasonable expectation of successfully administering a therapeutically effective amount of a corticosteroid to the upper gastrointestinal tract using an ODT. Dohil teaches that a specific volume (8-12mL) of a viscous liquid formulation is required to achieve pan-esophageal coverage and treat EoE. EX1002, [0067] (“It may have advantages over other therapies in that it is palatable, its volume (8-12ml) provides pan-esophageal mucosal coverage and it requires only once daily administration.”). As discussed above in Section VII.A, an ODT that

disintegrates within 60 seconds or 30 seconds would not achieve the volume that Dohil teaches provides pan-esophageal coverage and is efficacious. It would only produce 2-5mL saliva, which would not achieve pan-esophageal coating and would not reasonably be expected to be efficacious based on Dohil. EX2005, 303 (the rate of saliva “increases to about 4[.]0-5[.]0 ml / min during eating, chewing and other stimulating activities.”). Therefore, there would be no reasonable expectation of success. EX2007, ¶¶ 122-123.

a. Dohil and Venkatesh Do Not Render Obvious Claims 5-15, 20

Petitioner cites to Venkatesh’s disclosure of rapidly dispersing microgranules and drug particle size. Pet., 53-64. For the reasons discussed above in Section IX.A.2.a, Dohil and Venkatesh do not disclose an ODT containing a topical corticosteroid that is deposited topically on the upper gastrointestinal tract as claimed by the ’407 patent. Venkatesh’s taste-masking layer would prevent the corticosteroid from being topically deposited in the upper gastrointestinal tract and thus could not treat inflammation of the upper gastrointestinal tract. Thus, there would be no motivation or reasonable expectation of success to combine Dohil and Venkatesh to arrive at claims 5-15 and 20. EX2007, ¶ 149.

B. Grother and the FDA Guidance do Not Render the Claimed ODT Obvious

In Grounds 2 and 4, Petitioner relies on Grother, the FDA Guidance, and Venkatesh to challenge claims 1-4, 16-19, 21, 23-25, 27-42 and 5-15, 20 and 26, respectively. A POSA had no motivation or reasonable expectation of success in formulating the claimed ODT to treat inflammation (e.g., EoE), because neither Grother nor the FDA guidance suggest that an ODT can topically deposit a topical/non-systemic drug on the upper gastrointestinal tract. EX2007, ¶¶ 124-134. Venkatesh does not cure these deficiencies because Venkatesh's drug particles are coated with a taste-masking layer, which prevents the corticosteroid from being topically deposited on the upper gastrointestinal tract. EX2007, ¶¶ 150-159. Thus, Petitioner's Grounds 2 and 4 fail and claims 1-21 and 23-42 are patentable.

1. Grother and the FDA Guidance are General References and Do Not Teach or Suggest the ODT as Required By Claims 1-4, 16-19, 21, 23-25, 27-42

Petitioner argues that Grother discloses fast dispersing dosage forms that contain budesonide. Pet., 36-37. Petitioner points to Grother's disclosure that "[a]ny drug may be used as the active ingredient in the composition of the present invention," which includes budesonide. Pet., 36 (citing EX1008, 15:19-20, 18:15-18). As laid out above, Grother is not directed to any disease, but rather focused on eliminating mammalian gelatin from its disclosed fast dispersing solid dosage forms.

EX2011, 75:5-10, 79:1-10; EX1008, Abstract. A POSA would therefore understand that Grother discloses a general ODT platform for which any drug could be used as an active ingredient. EX1008, 15:19-20; EX2007, ¶ 126.

While Grother lists corticosteroids among hundreds of drugs, Grother also does not highlight the topical corticosteroids it lists or distinguish between systemically acting drugs from topically acting drugs with no systemic activity. EX2011, 78:4-18. To the contrary, Grother comingles topically acting corticosteroids with systemically acting corticosteroids that are excluded by the claims. *Compare* EX1001, 3:30-33 *with* EX1008, 18:15-18. Notably, Grother does not teach or suggest that its fast dispersing dosage form is capable of topically depositing a topically acting drug on the upper gastrointestinal tract. EX2011, 75:5-10; 79:1-10. To the contrary, Grother teaches that the ODTs can promote systemic absorption through the oral mucosa. *Supra*, Section VII.B. This teaching, and thus Grother, are irrelevant because budesonide has no significant systemic activity. Thus, nothing in Grother points to formulating an orally dispersing tablet with a topical corticosteroid, let alone budesonide, for the treatment of inflammation of the upper gastrointestinal tract or EoE. A POSA would thus understand that Grother did not recognize, and therefore did not teach or suggest, that orally disintegrating compositions could be used to topically administer budesonide to the upper gastrointestinal tract or esophagus for the treatment of EoE. EX2007, ¶ 126.

The FDA Guidance does not cure this deficiency in Grother. Rather, as explained above and as acknowledged by Petitioner's expert, the FDA Guidance merely provides a definition of ODTs. EX2011, 56:15-21. The FDA Guidance does not address any particular disease, such as EoE, any particular class of drugs, such as corticosteroids, or recognize the use of ODT to topically deposit topically acting drugs on the upper gastrointestinal tract. EX2011, 55:14-23. All the FDA Guidance does, therefore, is provide a POSA with the general definition of ODTs. EX2011, 56:15-21. The generalized disclosures in Grother and the FDA Guidance therefore cannot disclose the required claim limitations of the '407 patent. EX2007, ¶¶ 126-131.

2. No motivation to formulate the claimed ODT based on Grother in view of the FDA Guidance – No Recognition that an ODT could topically deposit a corticosteroid on the Upper Gastrointestinal Tract

Petitioner again uses impermissible hindsight to support its conclusory arguments for motivation to combine. As explained above, a POSA would have understood Grother to disclose a general ODT platform that is not directed to any disease or particular drug, and does not teach or suggest using an ODT to topically deposit a topically active drug on the upper gastrointestinal tract. EX2007, ¶ 126. Similarly, a POSA would understand the FDA Guidance to supply a definition for ODTs, and not teach or suggest using an ODT to topically deposit a topically active

drug on the upper gastrointestinal tract. EX2007, ¶ 93, 132; EX2011, 56:15-21. Petitioner argues that a POSA “would have been motivated to select budesonide as an active ingredient in Grother’s fast dispersing solid dosage form based on Grother’s express disclosure to do so.” Pet., 36. Petitioner asserts that this would not require a “leap of inventiveness.” Pet., 36 (citing *Boston Sci. Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982, 991 (Fed. Cir. 2009)). But Petitioner misstates the law. The law actually states that “[d]isparate embodiments in one reference can only be combined if they are a ‘predictable variation’ of each other that does not ‘require a leap of inventiveness.’” *Apple Inc. v. Corephotonics, Ltd.*, Case IPR2018-01348, 2019 WL 3714167, at *2 (P.T.A.B. Aug. 5, 2019) (Paper 11) (quoting *Boston Sci. Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982 (Fed. Cir. 2009)). But the drugs in Grother are not predictable variations.

Grother cites hundreds of drugs across six pages. EX1008, 16-21. While corticosteroids are listed, Grother does not highlight them in any way or distinguish between systemic and topical corticosteroids. EX1008, 18:15-18. Rather, systemic and topical corticosteroids are contained in the same list, with no distinction. *Id.* The drugs in Grother span a vast variety of drug classes, from analgesics to vaccines and stimulants, the overwhelming majority of which are systemically active and are absorbed through the lower gastrointestinal tract. *Id.* Petitioner does not and cannot argue that the various drugs listed in Grother are “predictable variations” of each

other. This is particularly true where budesonide and fluticasone act topically, whereas nearly all other drugs are systemically active and must be adsorbed in the blood stream in order to provide a therapeutic effect. Because of the wide array of drugs disclosed, and the lack of guidance on formulating an ODT with a topically acting drug for topical deposition on the upper gastrointestinal tract, the Petitioner's arbitrary selection of budesonide cannot be a "predictable variation," and Patent Owner's claims involve a leap of inventiveness. EX2007, ¶¶ 128-131.

It is clear that Petitioner has arbitrarily picked budesonide from Grother's non-limiting list simply because these drugs are recited in the claims of the '407 patent. EX2007, ¶ 130. The "rationale ... that a person of ordinary skill would 'pick and choose' features from various embodiments of [a single reference], simply because they are in the same [reference], is insufficient to demonstrate a reasonable likelihood of prevailing on this challenge[.]" *LG Display Co. v. Innovative Display Techs. LLC*, Case IPR2014-01362, Paper 12, at 13 (P.T.A.B. Mar. 2, 2015).

Petitioner's reliance on the FDA Guidance does not provide the requisite motivation that is absent from Grother. Instead of offering any explanation, Petitioner recites that a "POSA seeking to formulate budesonide into an orally disintegrating pharmaceutical composition would be highly motivated to follow the FDA Guidance that such a composition should disintegrate within 30 seconds or less when tested using the USP <701> Disintegration Test." Pet., 40. As discussed

above in Section VII.E, Petitioner does not explain why a POSA would be motivated to formulate fluticasone or budesonide in an ODT that disintegrates within 30 seconds using the USP <701> Disintegration Test for topical deposition of budesonide on the upper gastrointestinal tract in the first place. The FDA Guidance does not remedy this deficiency because the FDA Guidance is silent regarding topical corticosteroids, topical deposition of any active on the upper gastrointestinal tract, or topical treatment of inflammation of the upper gastrointestinal tract. The Petitioner's conclusory statements must be rejected. "To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness." *In re Magnum*, 829 F.3d at 1380.

Because Grother fails to recognize that ODTs can be used to topically administer a therapeutically effective amount of a topical drug to the upper gastrointestinal tract, and the FDA Guidance is silent regarding topical corticosteroids and topical treatment of the upper gastrointestinal tract, a POSA would not have been motivated to formulate an ODT with budesonide as asserted by Petitioner's argument. For this reason, Grounds 2 and 4 must fail.

a. Venkatesh does Not Cure the Deficiencies in Grother and the FDA Guidance

Petitioner asserts in Ground 4 that claims 5-15, 20, and 26 are unpatentable

over Grother, the FDA Guidance, and Venkatesh. As set out above, a POSA had no motivation to formulate an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet containing a topical corticosteroid that is topically deposited on the upper gastrointestinal tract based on the disclosure in Grother and the FDA Guidance. Venkatesh does not cure these deficiencies, because a POSA also would not have been motivated to combine the teachings in Venkatesh with the formulation in Grother and the FDA Guidance to arrive at the claimed invention. Petitioner continues to rely on impermissible hindsight. EX2007, ¶¶ 150-154.

As explained above, in Section IX.A.2.a, Venkatesh is not directed to a particular disease, the delivery of corticosteroids, or topical delivery of drugs. Instead, Venkatesh is directed generally to taste-masking of bitter drug particles administered using an ODT, as confirmed by Petitioner's expert. EX2011, 90:13-92:18, 93:12-16, 94:4-25; EX1020, [0013]. Based on this alone, a POSA would not consider Venkatesh to be relevant to the claims of the '407 patent and would not be motivated to combine Venkatesh with Grother and the FDA Guidance, and arrive at the claimed invention. Moreover, for the same reasons discussed for Ground 3, Petitioner fails to address Venkatesh's taste-masking, much less articulate a motivation to remove this essential feature from Venkatesh's ODT.

Neither Petitioner nor its expert explain why a POSA would be motivated to look to Venkatesh. Instead, Petitioner merely states that a POSA would have been

motivated to manufacture Grother's fast dispersing solid dosage form according to Venkatesh. Pet., 65. Because Petitioner's arguments regarding the alleged motivation to combine Grother and the FDA Guidance with Venkatesh are conclusory and do not explain any benefit to combining the references, they must be rejected. *See In re Magnum*, 829 F.3d at 1380 (declaring that "a petitioner cannot employ mere conclusory statements"). A POSA had no expectation of success based on Grother and the FDA Guidance alone or in combination with Venkatesh.

Petitioner does not even attempt to explain why a POSA would have a reasonable expectation of success in formulating an orally disintegrating pharmaceutical composition containing budesonide or fluticasone that would topically deposit budesonide or fluticasone on the upper gastrointestinal tract based on Grother's disclosure and the FDA Guidance. The most Petitioner can offer is that formulating orally disintegrating pharmaceutical compositions were routine at the time of the '407 patent. Pet., 40. But Petitioner's expert was not able to identify a single prior art ODT containing a topically acting drug that was deposited topically to the upper gastrointestinal track. EX2011, 17:8-15. Grother fails to recognize that an ODT can topically deposit a topically acting drug, such as a corticosteroid, to the upper gastrointestinal tract. As Petitioner's expert acknowledges, the FDA Guidance only provides a definition for ODTs, and thus does not remedy the deficiencies in Grother. EX2011, 56:15-21. Therefore, Petitioner failed to provide

any actual evidence that a POSA would arrive at the claimed invention with a reasonable expectation of success.

A POSA would understand that formulations for administering systemic drugs, which are absorbed by the lower gastrointestinal tract, differ from formulations that topically administer the drug to a localized area to the upper gastrointestinal tract. EX2007, ¶ 132. A POSA would therefore not reasonably expect to successfully formulate an orally disintegrating pharmaceutical composition containing a corticosteroid to topically deposit the corticosteroid on the upper gastrointestinal tract for treating inflammation of the upper gastrointestinal tract from Grother's disclosure and the FDA Guidance.

Venkatesh does not cure the deficiencies in Grother and the FDA Guidance. Petitioner relies on conclusory assertions that a POSA would have a reasonable expectation of success based on the process disclosed in Venkatesh. Pet., 66-68. Again, Petitioner does not attempt to explain how a POSA would have a reasonable expectation of success in arriving at the claimed invention based on Venkatesh's process, which coats the drug with a water-insoluble or pH-responsive taste-masking layer so that the drug does not contact the mouth or the upper gastrointestinal tract, or why a POSA would have a reasonable expectation of success in removing this essential feature from Venkatesh's composition and still achieve a pleasant tasting formulation.

Because Venkatesh's taste-masking layer would prevent a corticosteroid from contacting the upper gastrointestinal tract, there is no reasonable expectation of formulating an orally disintegrating composition to topically deposit a topically acting corticosteroid on the upper gastrointestinal tract to treat EoE based on Venkatesh, Grother, and FDA Guidance. EX2007, ¶ 158.

b. Grother and the FDA Guidance Do Not Render Obvious the Claimed Doses (Claims 1[ii], 35[i], 33-34)

Grother does not disclose the specific dose ranges required by claims 1[ii], 35[i], and 33-34. Petitioner cites to Grother's disclosure of general dosing, and that the "upper value" is generally 60 mg. Pet., 36. The dosages disclosed in Grother relate to dosing generally, not topically active corticosteroids specifically, and certainly not for a corticosteroid that is topically deposited on the upper gastrointestinal tract to treat inflammation or EoE. None of the unasserted references discussing budesonide disclose an ODT containing budesonide, and nearly all references involve enterically coated compositions that are designed to prevent budesonide release until the drug reaches the lower gastrointestinal tract or liquid formulations. Pet., 36-37. A POSA would understand that formulating an ODT to topically deposit a corticosteroid in the upper gastrointestinal tract would involve different considerations and likely different doses than liquid formulations, as well as enterically coated tablets and rectal foam dosage forms used for different

conditions. Petitioner fails to explain how Grother discloses the claimed doses for an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet containing a topical corticosteroid based on its general disclosures. EX2007, ¶¶ 133-134.

As discussed above, a POSA would not have any motivation or reasonable expectation of success to formulate an orally dispersing tablet containing budesonide with the claimed doses based on Grother and the FDA guidance (which does not disclose any dose for any drug). Petitioner's expert conclusively states that a POSA would have a reasonable expectation of success, but does not explain why or how. Pet., 37. For at least this reason, Petitioner's arguments must be rejected. *See In re Magnum*, 829 F.3d at 1380 (declaring that "a petitioner cannot employ mere conclusory statements").

b. Grother Does Not Disclose the Claimed Methods for Treatment (Claims 1-4, 16-19, 21, 23-25, 27-34)

Grother does not disclose the method disclosed in claims 1-4, 16-19, 21, 23-25, and 27-34 of the '407 patent. As discussed above, Grother does not disclose any disease and therefore cannot disclose methods of treating inflammation of the upper gastrointestinal tract recited in claims 1-4, 16-19, 21, 23-25, and 27-34 by administering an ODT. Thus, Petitioner has failed to establish *prima facie* obviousness for these claims, because all claim limitations are not taught by the

asserted references.

There would also be no reasonable expectation of success in treating the inflammation of the upper gastrointestinal tract recited in claims 1-4, 16-19, 21, 23-25, and 27-34 by administering an orally dispersing tablet. As discussed above and illustrated through Petitioner's evidence, previous solid formulations of budesonide largely involved enterically coated tablets for treating inflammation of the lower gastrointestinal tract. EX1025, EX1009, EX1010, EX1011, EX1012, EX1013, EX1026, EX1027, EX1028. There is no evidence in Grother, or the background art, that an ODT would or even could deposit a therapeutically effective amount of budesonide on the upper gastrointestinal tract to treat inflammation as required by the claims. Therefore, there would be no reasonable expectation of success.

a. Grother, the FDA Guidance and Venkatesh Do Not Render Obvious Claims 5-15, 20, 26

Petitioner cites to Venkatesh's disclosure of rapidly dispersing microgranules and drug particle size and argues it renders obvious claims 5-15, 20, and 26. Pet., 64-71. As described above, Venkatesh's rapidly dispersing microgranules and drug particle sizes are used for ODTs containing taste-masked drugs for the purposes of improving taste and mouth feel. Taste-masking would prevent the corticosteroid from being topically deposited in the upper gastrointestinal tract. As such, the combination of Grother, the FDA Guidance, and Venkatesh would not result in the

claimed invention. There would be no motivation to combine Grother, FDA Guidance and Venkatesh to arrive at claims 5-15, 20, and 26, or a reasonable expectation of success, for the reasons described above. EX2007, ¶ 160.

X. OBJECTIVE INDICIA OF NONOBVIOUSNESS

Secondary considerations also establish that the claims of the '407 patent are not obvious as of the priority date, including unexpected results.

A. Unexpected Results

PO's clinical trials show that ODTs containing 1.5 mg and 3 mg of fluticasone are therapeutically effective and well-tolerated, further supporting the non-obviousness of the invention. EX2002. As discussed above, Dohil teaches that 8-12mL of a viscous liquid formulation provides pan-esophageal coating and delivers an effective dose of budesonide to the esophagus to treat EoE, whereas the claimed ODT would not produce 8-12mL. EX1002, [0067]. Consequently, a POSA would not have expected an ODT that disintegrated in the mouth within 60 seconds to be efficacious. EX2007, ¶ 162.

However, a clinical study funded by Petitioner comparing the claimed ODT to Dohil's liquid showed that the ODT was equally efficacious, even at half the corticosteroid dose, which is surprising and unexpected. EX2006. Petitioner's study compared the claimed orally dispersing tablet to a 5ml viscous solution containing budesonide (dosed twice a day, for a total of 10ml viscous solution), such as the one

disclosed in Dohil. EX2006, 2. The study found that “interestingly,” patients who received the tablet of 1 mg of budesonide twice daily achieved remission, similar to patients who received the viscous solution of 2 mg of budesonide twice daily. EX2006, 8. The study concluded that “no additional benefit could be shown for the higher dose of . . . budesonide [tablet] (2 mg twice daily) used in our study compared with previous studies examining viscous suspensions.” EX2006, 8. Based on the known efficacy of the viscous liquid formulations of budesonide, administered twice a day at a volume of 5ml, for a total of 10ml, or 8-12ml as disclosed in Dohil, a POSA would not have expected an ODT that produces only 1-2ml of solution and uses half the budesonide dose to be efficacious in providing the necessary pan-esophageal coverage in order to effectively treat EoE. EX2007, ¶¶ 163-164.

Further, a POSA would have known that oral corticosteroid administration causes candidiasis, and the longer the corticosteroid is held in the mouth, the greater the chance of candidiasis developing. A POSA would have been deterred from developing an ODT that would be held in the mouth longer than a liquid (which is swallowed immediately) because it would have been expected to increase the rate of candidiasis infections. Surprisingly, PO’s study found that patients who received 1.5 and 3 mg of fluticasone once daily achieved remission, with low rates of candidiasis, compared to patients receiving fluticasone twice daily. EX2002, 7. Also surprisingly, patients receiving 1.5 and 3 mg of fluticasone once daily showed

equal or superior improvement in clinical symptoms compared to twice daily treatment. EX2002, 7-9. EX2007, ¶ 165.

XI. CONCLUSION

For the foregoing reasons, Petitioner has failed to establish that the challenged claims of the '407 patent are unpatentable. Patent Owner respectfully requests the Board find the challenged claims patentable over the grounds in the Petition.

Date: September 9, 2025

Respectfully submitted,

Cooley LLP
ATTN: Patent Group
1299 Pennsylvania Ave., NW
Suite 700
Washington D. C. 20004
Tel: (202) 776-2982
Fax: (202) 842-7887

BY: /Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390
Counsel for Patent Owner

CERTIFICATE OF COMPLIANCE WITH WORD COUNT

Pursuant to 37 C. F. R. § 42. 24(d), I certify that this response complies with the type-volume limits of 37 C. F. R. § 42. 24(c)(1) because it contains 12,232 words, according to the word-processing system used to prepare this petition, excluding the parts of this response that are exempted by 37 C.F.R. § 42.24(c) (including the table of contents, a table of authorities, an exhibits list, a listing of facts, a certificate of service or this certificate of word count, or appendix of exhibits).

Date: September 9, 2025

Respectfully submitted,

Cooley LLP
ATTN: Patent Group
1299 Pennsylvania Ave., NW
Suite 700
Washington D. C. 20004
Tel: (202) 776-2982
Fax: (202) 842-7887

BY: /Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390
Counsel for Patent Owner

**CERTIFICATION OF SERVICE
UNDER 37 C. F. R. §§ 42. 6(e), 42. 105(a)**

I, Sanya Sukduang, hereby certify that on September 9, 2025, the foregoing Patent Owner's Response and Exhibits 2002-2023 pursuant to 37 C. F. R. § 42.8 were served electronically via email on the following counsel of record for Petitioner as follows:

Nathanael Luman
Eric S. Furman
Philip J. Minnick
KNOBBE, MARTENS, OLSON, & BEAR, LLP
2nrl@knobbe. com
2esf@knobbe. com
2pjm@knobbe. com
BoxDRFPGL.001LP@knobbe. com

DATED: September 9, 2025

/Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390