

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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INTAS PHARMACEUTICALS LTD.,  
Petitioner,

v.

ATOSSA THERAPEUTICS, INC.,  
Patent Owner

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Case PGR2025-00043  
Patent 12,071,391

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**PATENT OWNER'S CONTINGENT MOTION TO AMEND  
UNDER 37 C.F.R. § 42.221 INCLUDING  
REQUEST FOR PRELIMINARY GUIDANCE**

**LIST OF EXHIBITS**

<b>Exhibit</b>	<b>Description</b>
EX2001	ATOSSA THERAPEUTICS, INC. QUARTERLY REPORT FORM 10-Q (March 31, 2025)
EX2002	Atossa Therapeutics Proposes Potentially Groundbreaking Study Aimed at Reducing Interval Breast Cancer in High-Risk Women at AACR 2025 (April 29, 2025)
EX2003	Atossa Therapeutics Announces Plans to Pursue Metastatic Breast Cancer Indication for (Z)-Endoxifen and Continued Engagement with FDA on Additional Indications (March 11, 2025)
EX2004	Financials – Intas Pharmaceuticals Ltd., <a href="http://www.intas-pharma.com/financials/">http://www.intas-pharma.com/financials/</a>
EX2005	Atossa Therapeutics Announces Issuance of Key U.S. Patent Covering Endoxifen (March 08, 2022)
EX2006	Efficacy and Safety of Endoxifen in Bipolar I Disorder Patients, NCT06608641 (Last Updated March 17, 2025), <a href="https://clinicaltrials.gov/study/NCT06608641">https://clinicaltrials.gov/study/NCT06608641</a>
EX2007	Declaration of Sayem Osman
EX2008	Atossa Covenant Not to Sue
EX2009	Atossa Therapeutics Announces Full Results from Phase 2 KARISMA-Endoxifen Study Demonstrating Statistically Significant Reductions in Mammographic Breast Density (Dec. 11, 2024)
EX2010	Atossa Therapeutics Announces First Quarter 2025 Financial Results and Provides a Corporate Update (May 13, 2025)
EX2011	INTENTIONALLY OMITTED
EX2012	Breast Center Year in Review, An Unmet Need in HR-Positive Endocrine-Resistant Breast Cancer, <i>available at</i> <a href="https://jons-online.com/special-issues-and-supplements/2021/2021-year-in-review-breast-cancer/an-unmet-need-in-hr-positive-endocrine-resistant-breast-cancer">https://jons-online.com/special-issues-and-supplements/2021/2021-year-in-review-breast-cancer/an-unmet-need-in-hr-positive-endocrine-resistant-breast-cancer</a>
EX2013	ATOSSA THERAPEUTICS, INC. ANNUAL REPORT FORM 10-K for the Fiscal Year Ended December 31, 2024
EX2014	U.S. Patent No. 11,572,334
EX2015	Intas Requirements For Resolving Disputes With Atossa (FILED UNDER SEAL)

<b>Exhibit</b>	<b>Description</b>
EX2016	Default Protective Order
EX2017	<i>Intas Pharmaceuticals, Limited v. Atossa Therapeutics, Inc.</i> , IPR2025-00799, Pap.1 (Apr. 3, 2025)
EX2018	<i>Intas Pharmaceuticals, Limited v. Atossa Therapeutics, Inc.</i> , PGR2023-00043, Pap.1 (Aug. 18, 2023)
EX2019	Rishab Gupta & Swarndeeep Singh, <i>Endoxifen Approval for Bi-polar in India, A Premature or a Pragmatic Decision?</i> , 43(1) J. CLINICAL PSYCHOPHARMACOLOGY 3 (2023)
EX2020	Zonalta, Why Zonalta?, <a href="https://zonalta.in/">https://zonalta.in/</a>
EX2021	Atossa Therapeutics Granted Additional Patent Protection for Endoxifen (August 28, 2024)
EX2022	Declaration of Megan Raymond
EX2023	Corrected Covenant Not to Sue
EX2024	December 6, 2025, Collection of Email Communications with Intas's Counsel
EX2025	Declaration of Sayem Osman
EX2026	U.S. Patent No. 12,245,997
EX2027	Declaration of Jacob M. Berman
EX2028	Declaration of Han Xu
EX2029	Declaration of Hayley R. LeBlanc
EX2030	Declaration of Stephen Graham Davies, DPhil
EX2031	The Merriam-Webster Dictionary (2004)
EX2032	Transcript of January 16, 2026 Deposition of Jason McConville, Ph.D.
EX2033	Transcript of January 20, 2026 Deposition of Ron Bihovsky, Ph.D.
EX2034	Declaration of Sayem Osman
EX2035	INTENTIONALLY OMITTED
EX2036	INTENTIONALLY OMITTED
EX2037	INTENTIONALLY OMITTED
EX2038	INTENTIONALLY OMITTED
EX2039	INTENTIONALLY OMITTED
EX2040	INTENTIONALLY OMITTED
EX2041	INTENTIONALLY OMITTED
EX2042	INTENTIONALLY OMITTED
EX2043	INTENTIONALLY OMITTED
EX2044	INTENTIONALLY OMITTED
EX2045	INTENTIONALLY OMITTED

<b>Exhibit</b>	<b>Description</b>
EX2046	INTENTIONALLY OMITTED
EX2047	INTENTIONALLY OMITTED
EX2048	INTENTIONALLY OMITTED
EX2049	INTENTIONALLY OMITTED
EX2050	William E. Brown & Margareth R. Marques, <i>USP and Dissolution—20 Years of Progress</i> , Dissolution Technologies (2014)

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## **I. Introduction**

Pursuant to the Board’s Jan. 16, 2026 Order (Pap.33, “Order”), Atossa Therapeutics, Inc. (“PO”/“Atossa”) respectfully submits this §42.221(a)<sup>1</sup> Contingent Motion to Amend U.S. Patent No. 12,071,391 (“’391 Patent”). Should the Board find any of original claims 1-44 unpatentable, PO respectfully requests that the Board grant this Motion and issue the corresponding proposed substitute claim(s) presented herein.

## **II. Statement Of Relief Requested**

PO respectfully requests preliminary guidance on this Motion pursuant to §42.221(e). PO only seeks to amend claim 1-44 if the Board finds them unpatentable. A listing of the claims is attached hereto as Appendix A pursuant to §42.221(b).

## **III. Legal Standards**

A motion to amend must: (1) propose a reasonable number of substitute claims (§42.221(a)(3)); (2) propose substitute claims that do not enlarge the scope of the claims or introduce new subject matter (§42.221(a)(2)(ii)); (3) respond to a ground of unpatentability involved in the trial (§42.221(a)(2)(i)); and (4) set forth written description support for each substitute claim (§42.221(b)(1)). *Lectrosonics, Inc. v. Zaxcom, Inc.*, IPR2018-01129, Pap.15, 4-8 (Feb. 25, 2019) (precedential)

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<sup>1</sup> Unless stated, statutory and regulatory citations are to 35 U.S.C. or 37 C.F.R., as context indicates, internal citations omitted, and emphases/annotations are added.

(“*Lectrosonics*”). “[A] patent owner does not bear the burden of persuasion to demonstrate the patentability of substitute claims presented in a motion to amend.” *Id.* at 4. “[T]he burden of persuasion ordinarily will lie with the petitioner to show that any proposed substitute claims are unpatentable by a preponderance of the evidence.” *Id.*

#### **IV. The Number Of Proposed Claims Is Reasonable**

PO proposes one substitute claim to replace each original claim. Thus, the requirement of proposing a reasonable number of substitute claims has been met. *See* §326(d)(1)(B); §42.221(a)(3).

#### **V. The Proposed Claims Respond To Patentability Grounds And Do Not Enlarge The Claim Scope Or Introduce New Matter**

As set forth in detail below, each proposed Substitute Claim responds to a patentability ground raised in the above-captioned Petition (“Petition”/“Pet.”),<sup>2</sup> does not enlarge the scope of the claims or introduce new subject matter, and is supported by, *e.g.*, U.S. Patent App. No. 18/128,536 (“’536”; EX1002, 7-142), which was filed

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<sup>2</sup> PO does not separately address “responsiveness” for Substitute Claims 47-48, 53-57, 64-68, 72-74, 78-81, 84-86, and 88, as the only change from the original dependent claim is to update the claim’s dependency to reflect the substitute base claim.

on March 30, 2023 and issued as the '391 Patent.<sup>3</sup> In addition to the exemplary support discussed below, PO also sets forth additional support in Table 1 below.<sup>4</sup>

Substitute Claim #	'536 Application (EX1002 pp. 7-142)
45	¶¶10-11, 36, 169, 199, 184, 195, 199, 211-213, 215, 296, 298, cls. 1, 2
46	¶¶76, 151-152, 184-185, 317
47	¶¶33, 151, 154-166, 185-189, 246, 250, 256, 258-259, 263, 318-321, cl. 125
48	¶¶14, 16, 21, 36, 44, 214, 302-04, 361-366, 472, cls. 36, 40, 59, 133, 137, 154,
49	¶¶14, 16, 36, 44, 71, 167, 195-196, 203, 211, 214-215, 300, 361-366, cls. 34, 131
50	¶¶14, 16, 21, 36, 44, 49-51, 71, 167, 195, 199, 211, 216-217, 300-302, 361-366, cls. 34, 36, 40, 59, 131, 133, 137, 154
51	¶¶12-13, 18, 21, 42, 44, 149, 172, 175, 178, 225-226, 263, 283, 289, 292, 303-304 334-335, 446, 350

<sup>3</sup> The material prior art known to PO is the art cited in this proceeding, the related PTAB proceedings (IPR2025-00799, PGR2023-00043), and the prior art PO has disclosed to the Office during prosecution of the '536 Application and all family members relating to the '391 Patent, and the prior art cited by the Office in these patent applications.

<sup>4</sup> The '391 Patent claims priority to earlier applications and provisional applications. Because all of the prior art at issue in the Petition pre-dates the earliest provisional applications, PO is not currently seeking to have the Board give it the benefit of the filing date of any of the earlier applications. PO reserves the right to claim priority to these earlier applications if priority becomes an issue. *See* Order at 7.

52	¶¶199, 215 296, 298 314
53	¶¶195, 300
54	¶¶195, 300
55	¶¶75, 195, 197, 232, 236, 298, 429, 431-432, Table 12
56	¶¶191, 195, 199, 205-207, 212-213, 298, 429, 431-432, Table 12
57	¶¶429, 431-432, Table 12
58	¶¶195, 197, 199, 205-206
59	¶¶197, 199, 201, 206, 209
60	¶¶ 149, 432-34, Table 13
61	¶¶44, 225-228, 230, 303-304, 308-309, 313
62	¶¶225-227, 303-304
63	¶¶18-19, 43-44, 219, 225, 228-230, 265, 309-310, 313
64	¶¶199, 200
65	¶¶75, 199, 201-202, 296, 314
66	¶¶199, 201
67	¶¶199, 203-205, 296, 314
68	¶¶199, 206, 296, 314
69	¶¶199, 206 (explicitly disclosing “ethyl laureate”), 296, 314
70	¶¶11-14, 18, 21, 42, 44, 172, 175, 178, 263, 291, 292, 334-335, 350, cls. 11, 22, 31, 50, 57, 147, 152
71	¶¶11-13, 18, 21, 42, 44, 172, 175, 178, 263, 292, 334-335, 350, cls. 11, 22, 31, 50, 57, 147, 152
72	¶¶221, 223-224, 267, 269-270, 471-472, Tables 16-17, Figs. 3-8
73	¶¶263, 350, Table 22
74	¶¶75, 191, 195, 197, 199, 205-207, 212-213, 232, 236, 296, 298, 300, 429, 431-432, Table 12
75	¶¶195, 199, 206, 212-213, 236, 296, 298, 300, 429, 431-432, Table 12
76	¶¶10-11, 36, 169, 190-191, 195, 199, 212-213, 215, cls. 1, 2
77	¶¶11-13, 18, 21, 42, 44, 172, 175, 178, 263, 292, 334-335, 350, cls. 11, 22, 31, 50, 57, 152, cls. 11, 22, 31, 50, 57, 147, 152
78	¶¶ 221, 223-224, 267, 269-270, 471-472, Tables 16-17, Figs. 3-8
79	¶¶263, 350, Table 22
80	¶¶15, 18-19, 38, 43-44, 248, 253, 257-258, 260-261, 337, 352-354, 359-366, 372, 488, 499, Table 22, Fig. 3, cls. 38, 51, 54, 135, 148, 151
81	¶¶15, 18-19, 38, 43-44, 248, 253, 257-258, 260-261, 337, 352-354, 359-366, 372, 488, 499, Table 22, Fig. 3, cls. 38, 51, 54, 135, 148, 151

82	¶¶225-227, 303-304
83	¶¶18-19, 43-44, 219, 225, 228-230, 265, 309-310, 313
84	¶¶21, 37, 44, 224, 270, 366, Table 17, cls. 42, 58, 139, 153
85	¶¶468, 472, 477, 479, Table 19C
86	¶¶9, 14, 17-20, 38-39, 41-44, 63, 80, 86, 96-97, 237-241, 246, 248, 250, 254, 259-262, 272, 275, 322-329, 333, 339, 344-345, 349, 359-367, 371-373, cls. 37, 44, 45, 47, 54, 55, 134
87	¶¶9, 17, 20, 39, 44, 86, 239, 241, 323, 329, 345, 360-366, 372, cls. 44-45, 55, 142, 157
88	¶¶17, 41, 245-246, 249-251, 254-57, 326, 333, 349, 372, 491-493, 496-500, cls. 47, 144.

**Substitute Claims 45, 76**: PO’s proposed Substitute Claims 45 and 76 amend original independent claims 1 and 32, respectively, to additionally require that “**the endoxifen and the enteric material are mixed together.**” This added limitation makes explicit the meaning of “[a] composition comprising an endoxifen and an enteric material” recited in the original preamble. *See, e.g., PIN/NIP, Inc. v. Platte Chemical Co.*, 304 F.3d 1235, 1244 (Fed. Cir. 2002) (holding that “we equate[] a ‘composition’ with a ‘mixture,’” and that “a chemical composition exists at the moment the ingredients are *mixed together*”) (emphasis original); *Exxon Chemical Patents, Inc. v. Lubrizol Corp.*, 64 F.3d 1553, 1557-58 (Fed. Cir. 1995); *Mars, Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1373-74 (Fed. Cir. 2004).

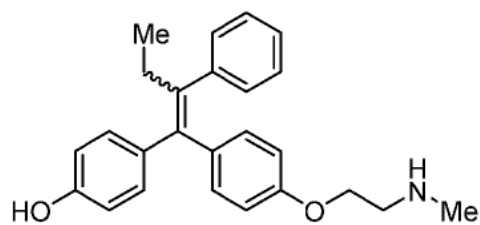
Substitute Claims 45 and 76 are responsive to and patentable over Grounds 1 and 2, the only Grounds that challenge the independent claims. In Ground 1 (anticipation), Petitioner contends that Ahmad discloses “[a] composition comprising an endoxifen and an enteric material” because Ahmad discloses that “composition

containing endoxifen...can be *encapsulated in enteric-coated capsules.*” Pet. 20 (citing EX1003, 18:19–21). Ground 2 (obviousness) does not offer any new theories and rests on a single throwaway paragraph that fails to even identify the specific claim element(s) Petitioner contends may be missing from Ahmad.

Ahmad does not disclose the proposed “mixed together” limitation. Ahmad’s relevant disclosure is directed to applying a separate enteric coating to the outside of a capsule that is already “filled with composition containing endoxifen,” explaining that “[e]nteric coating of capsules filled with composition containing endoxifen can be done as methods known in the art.” EX1003, 18:19-29. That is an external coating step on a composition containing only endoxifen, not a disclosure of an enteric material that is mixed together with endoxifen in the composition itself.

Accordingly, Substitute Claims 45 and 76 are responsive to and patentable over Grounds 1 and 2 because the added limitation directly narrows the independent claims to the specific configuration that Ahmad does not disclose.

**Exemplary Support for Substitute Claims 45, 76:** The ’536 discloses “a composition comprising a crystalline form of a compound of Formula (III):”



Formula (III).

EX1002, ¶10. “[A]t least 90% by weight of the compound of Formula (III) in the composition is the (Z)-isomer.” *Id.* ¶11. The ’536 provides “a composition comprising (Z)-endoxifen free base or a salt thereof.” *Id.* ¶36. Regarding the mixing of the endoxifen and the enteric material, the ’536 discloses a “composition” containing both elements and would be understood to indicate that the elements of the composition are mixed. *Id.* ¶¶195, 199, 212-213; *see also* EX2030, ¶35. The ’536 also states that, *e.g.*, the “enteric tablets... may be *uncoated*.” *Id.* ¶215; *see also* EX2030, ¶35. The ’536 further states “compositions of the present disclosure can be administered to a subject in need thereof,” and “the compositions comprising endoxifen further comprise an excipient. Such an excipient can be compatible with the intended route of administration.” *Id.* ¶¶ 190-91. Petitioner does not dispute that a “composition” would be understood to include (not exclude) internal mixtures of endoxifen and enteric material (*e.g.*, within a capsule or tablet). *See, e.g.*, Pap.10, 13-14 (“In short, claim 1 covers any enteric material—whether external *or internal*--that comprises part of the composition.”).

**Substitute Claim 46** narrows original claim 2’s recited salts to a subset, and is responsive to and patentable over Grounds 1-2, which rely on Ahmad. Pet.25-26. The amendment deletes the salt forms purportedly disclosed in Ahmad. **Support:** The ’536 describes that embodiments of the endoxifen salts as being selected from “the group consisting of ‘arecoline...bicarbonate...glutamate, glycollylarsanilate,

hexylresorcinate, hydrabamine...hydroxynaphthanoate, isethionate, malate, mandelate ... methyl sulfate, mucate ... pantothenate ... polygalacturonate ... stearate ... tannate, Teoclate, and triethiodide” and “benzathine, clemizole, chlorprocaine, choline, diethylamine, diethanolamine, ethylenediamine, meglumine, piperazine, procaine, aluminum, barium, bismuth, lithium, magnesium, potassium, and zinc.” EX1002, ¶¶151-152. Further, the ’536 describes endoxifen salt compositions selected from a group listing the same as described above. *Id.* ¶¶185, 317.

**Substitute Claim 47** is supported by the ’536, which states “the endoxifen comprised in a composition of the present disclosure is an endoxifen gluconate.” EX1002, ¶¶154, 259.

**Substitute Claim 48** is supported by the ’536, which states “[a] composition comprising a crystalline form of a compound of Formula (III) may be formulated for oral delivery as... a delayed-release tablet, a delayed-release caplet or a delayed-release capsule.” EX1002, ¶14.

**Substitute Claims 49** amends original claim 5’s recitation of “composition is a tablet” to “composition is *formulated as* an *uncoated* tablet.” This amendment is responsive to and patentable over Grounds 1-2, which rely on Ahmad’s disclosure of “[e]nteric *coating* of capsules.” Pet.27-28. As amended, this limitation cannot be met by Ahmad’s enteric *coating*-based disclosures. **Support:** The ’536 states “the composition is formulated as...[a] tablet.” EX1002, ¶¶16, 300, 167 (“pharmaceutical

compositions in different dosage or delivery forms, such as solid oral dosage forms including tablet.”). The “[c]ompositions intended for oral use may be *prepared in* solid or fluid unit dosage forms.” *Id.* ¶195. The ’536 further states that “the enteric tablets... may be *uncoated.*” *Id.* ¶215.

**Substitute Claim 50** amends original claim 6 (“composition is a capsule”) to “composition is *contained within* a capsule”, and is responsive to and patentable over Grounds 1-2, which rely on Ahmad’s disclosure of “[e]nteric *coating* of capsules.” Pet.27-28. As amended, this limitation cannot be met by Ahmad’s enteric *coating*-based disclosures because Ahmad fails to disclose an endoxifen-enteric material composition contained within a capsule. **Support:** The ’536 states “the composition formulated for oral delivery” may be formulated as a “capsule.” EX1002, ¶¶16, 300, 167 (“pharmaceutical compositions in different dosage or delivery forms, such as solid oral dosage forms including tablets and capsules.”); 195 (“Compositions intended for oral use may be *prepared in* solid or fluid unit dosage forms.”). The ’536 further states “*a composition* disclosed herein (for example, *in the same capsule*, tablet, ointment, etc.) or in separate compositions (for example, in 2 separate capsules).” *Id.* ¶71.

**Substitute Claim 51** (i) changes the dependency to Substitute Claim 49, thereby narrowing original claim 7’s limitation “composition is uncoated” (now deleted) to Substitute Claim 49’s “composition is formulated as an *uncoated tablet,*”

and (ii) adds similar stability, gastric release and dosage limitations (as individually found in Substitute Claims 60, 62 and 71, respectively). These amendments are responsive to and patentable over Ground 4, which relies on Ahmad's "enteric-coated *capsules*" disclosure combined with Benameur's "enteric *capsule* drug delivery technology" that provides enteric protection "without the use of coatings." Pet.54-55. Critically, neither reference discloses the claimed endoxifen-enteric composition formulated as an "*uncoated tablet*," nor the new dosage, stability and gastric release limitations. **Support:** The '536 states "the composition comprises about...20 mg of polymorphic Form III." EX1002, ¶178. The '536 further states that "the (Z)-endoxifen is stable at ambient temperature for...at least 18 months." *Id.* ¶¶283, 289. The '536 additionally discloses that "in other embodiments,...less than 50% of (Z)-endoxifen is released in the stomach after 6 hours of administration, as tested by a method of USP 711" *Id.* ¶226.

**Substitute Claim 52** amends original claim 8 to require the "enteric material comprises an enteric coating," and is responsive to and patentable over Grounds 1-2, which rely on Ahmad's disclosure of "[e]nteric coating of capsules." Pet.27. Substitute Claim 52 depends from Substitute Claim 45, which requires that the endoxifen and enteric material are mixed together in the claimed composition, and then additionally requires that the enteric material comprise an enteric coating (*i.e.*, surrounds (coats) the other component(s) of the composition (*e.g.*, the endoxifen)).

Ahmad does not disclose a formulation where the enteric functionality is supplied by an enteric material that coats the endoxifen with which it is mixed, as now required. **Support:** The '536 states “[e]xamples of excipients that can be used in the compositions...can include... control release agents, enteric coatings,...or any combination thereof.” EX1002, ¶199. It further identifies enteric materials that would mix with and coat endoxifen. *Id.* ¶298.

**Substitute Claim 53** is supported by the '536, which states “[c]ompositions intended for oral use may be prepared in ... fluid unit dosage forms” and “the compositions are formulated for oral delivery as...suspensions.” EX1002, ¶195; *see also* Substitute Claim 74, *infra*.

**Substitute Claims 54** is supported by the '536, which states “[c]ompositions intended for oral use may be prepared in...fluid unit dosage forms” and “the compositions are formulated for oral delivery as...elixirs, suspensions, syrups.” EX1002, ¶195. The '536 further states that the “composition...further comprises one or more excipient.” *Id.* ¶¶191, 199, 205-207, 212-213. Those disclosures convey possession of the recited suspension embodiments in which the suspension includes a fluid vehicle/excipient of the types expressly identified for fluid dosage forms. *See* EX2030, ¶¶72-74.

**Substitute Claim 55** is supported by the '536, which states “[c]ompositions intended for oral use may be prepared in...fluid unit dosage forms.” EX1002, ¶195. Petitioner itself asserts that “a suspension necessarily includes a fluid.” Pet.28.

**Substitute Claim 56** is supported by the '536, which states “(Z)-endoxifen free base is surprisingly stable in alcoholic (for example ethanol...) solutions.” EX1002, 432. The '536 further discloses “compositions” “*prepared in...fluid* unit dosage forms” (including “suspensions”), and that the “composition...*further comprises* one or more excipient.” EX1002, ¶¶191, 195, 199, 205-207, 212-213. Those disclosures convey possession of the recited suspension embodiments in which the suspension includes a fluid vehicle/excipient of the types expressly identified for fluid dosage forms. *See* EX2030, ¶¶72-74.

**Substitute Claim 57** is thus supported by the '536, which states “[t]he stability of (Z)-endoxifen free base Sample 1 of Table 11 was studied when stored at various temperatures in solid form and in ethanol (EtOH) solution.” EX1002, ¶¶429; 432 (“(Z)-endoxifen free base is surprisingly stable in alcoholic (for example ethanol...) solutions”); *see also* Substitute Claim 56.

**Substitute Claim 58** narrows original claim 14’s recitation of “the suspension comprises an alcohol, a plant oil, a mineral oil, a glycol, an agar, or a mixture thereof” to only “an **agar**.” This amendment is responsive to and patentable over Grounds 1-2 and 5, which rely on Ahmad and de Veilliers (Pet.29, 58-60), by

deleting the elements purportedly disclosed in Ahmad and de Veilliers. **Support:** The '536 discloses that “a pharmaceutical composition of the present disclosure is formulated for oral delivery.” EX1002, ¶195. Further, “the compositions are formulated for oral delivery as... suspensions.” *Id.* ¶195. The '536 discloses that “compositions designed for oral administration can be made with an inert or active excipient.” *Id.* ¶197. The '536 provides examples of various excipients, including “disintegrating agents” and “lubricants.” *Id.* ¶199. The '536 describes “[d]isintegrants that can be used in the pharmaceutical compositions...include...agar.” *Id.* ¶205. Additionally, the '536 describes “[l]ubricants that can be used in pharmaceutical compositions...include...agar.” *Id.* ¶206. Those disclosures convey possession of the recited suspension embodiments in which the suspension includes a fluid vehicle/excipient of the types expressly identified for fluid dosage forms. *See* EX2030, ¶¶72-74.

**Substitute Claim 59** narrows original claim 15's suspension recitation to a smaller subset reciting “sorbitol, mannitol, stearic acid, sodium lauryl sulfate, or a mixture thereof.” This amendment is responsive to and patentable over Grounds 1-2 and 5, which rely on Ahmad and de Veilliers (Pet.29-30, 58-60), by deleting the elements purportedly disclosed in Ahmad and de Veilliers. **Support:** As described in the support for Substitute Claim 58, the '536 discloses excipients used in compositions, including lubricants. EX1002, ¶¶197, 199. The '536 describes “[l]ubricants

that can be used in the pharmaceutical composition...include... sorbitol, mannitol...stearic acid, sodium lauryl sulfate...and mixtures thereof.” *Id.* ¶206.

**Substitute Claim 60** amends original claim 16’s limitation from “wherein the compound of Formula (III) is stable in the composition for at least **10 days** at about **25° C**” to “**3 months** at about **40° C**”. This amendment is responsive to and patentable over Ground 2, which relies on Elkins and Dr. Bihovsky’s testing. Pet.42-46. Petitioner acknowledges that a POSITA would have understood “stable” in this limitation to mean “the continued presence of at least **90% (Z)-endoxifen.**” Pet. 42-43. On the other hand, Elkins discloses “rapid degradation to **87%** at 40° C/75% RH in 3 months,” which is below the 90% “stable” requirement and thus does not disclose the amended requirement. Dr. Bihovsky likewise tested only **10 days** at 40° C, which does not supply the missing **3-month** at 40° C requirement. **Support:** The ’536 states “(Z)-Endoxifen prepared by the processes disclosed below is stable...for at least 3 months [sic] at 40 °C/75% RH (Example 9).” EX1002, ¶149. The ’536 further discloses a bulk drug stability study’s results in Table 13. *Id.* ¶¶433-434. The ’536 discloses that during the bulk drug stability study, samples of (Z)-endoxifen free base “were placed in tightly capped, 180 mL HDPE bottles under inert conditions (dry nitrogen)...at 40 °C/75% RH for 3 months.” *Id.* ¶433. Table 13 describes the purity of the (Z)-endoxifen at various time points with different storage conditions.

*Id.* ¶434. The reported results show that the temperature was at 40° C, the purity of (Z)-endoxifen was 99.5% at three months. *Id.* ¶434.

**Substitute Claim 61** amends original claim 17’s limitation from “resistant to dissolution in an acidic environment for at least **2** hours” to “at least **4** hours”. This is responsive to and patentable over Ground 7, which relies on Cole to purportedly teach “that its enteric coating prevents drug release for at least **two hours** under strongly acidic conditions.” Pet.69-70. Critically, Cole’s disclosure is explicitly limited to a “two hours,” and Cole does not disclose or measure the amount of drug released in an acidic environment for **at least 4 hours**. **Support:** The ’536 describes “dissolution tests according the current methods of USP 711.” EX1002, ¶225. During the dissolution tests, the ’536 Application describes “the oral dosage forms... are protected from the acidic environment of the stomach and do not dissolve for... at least 4 hours.” *Id.* ¶225. Relatedly, the ’536 discloses “the composition is formulated for oral delivery, and... as tested by a method of USP 711...the composition releases in the stomach... in 4 hours after administration.” *Id.* ¶¶303-304; *see id.* ¶313.

**Substitute Claim 62** amends original claim 18’s limitation from “the **composition releases** no more than **10%** of the (Z)-endoxifen over **2** hours in gastric fluid” to “no more than **40%** of the (Z)-endoxifen **is released** over **4** hours in gastric fluid.” This is responsive to and patentable over Ground 7, which relies on Cole to

purportedly disclose “that its enteric coatings would not release any drug for **2 hours** in gastric fluid or in the stomach.” Pet.70-71. Critically, Cole’s disclosure is explicitly limited to a **2-hour** exposure, and Cole does not disclose or measure the amount of drug released in a stomach over a **4-hour** period. **Support:** The ’536 describes “wherein less than 40% of (Z)-endoxifen is released in the stomach after 4 hours of administration...as tested by a method of USP 711.” EX1002, ¶¶226, 227 (“a composition disclosed herein releases in the stomach...less than 40% of (Z)-endoxifen in 4 hours after administration...as tested by a method of USP 711.”), 303-304.

**Substitute Claim 63** amends original claim 19 from “**the composition releases** at least 50% of the (Z)-endoxifen **within** 8 hours in intestinal fluid” to “at least 50% of the (Z)-endoxifen **is released after** 8 hours.” This is responsive to and patentable over Ground 7, which relies on Ahmad in view of Cole to purportedly disclose the original requirement of “within” 8 hours. Critically, Cole does not disclose any data on release of a drug in intestinal fluid “after” 8 hours. **Support:** The ’536 states “the composition is formulated to release in the small intestine, such that... at least 50% of endoxifen is released after 8 hours after administration, as tested by a method of USP 711.” EX1002, ¶228.

**Substitute Claim 64** is supported by the ’536, which states “[b]inders suitable for use in the pharmaceutical compositions provided herein include... hydroxypropyl methyl cellulose.” EX1002, ¶¶199, 200.

**Substitute Claims 65-66** are supported by the '536, which states “[e]xamples of fillers suitable for use in the pharmaceutical compositions provided herein include, but are not limited to, talc, calcium carbonate (e.g., granules or powder), sugars[,]... a salt such as calcium carbonate,... microcrystalline cellulose[,]... cellulosic bases such as methyl cellulose, carboxymethyl cellulose dextrans, kaolin, mannitol, silicic acid, sorbitol, starch, pre gelatinized starch, and mixtures thereof.” EX1002, ¶¶201, 199.

**Substitute Claims 67-68** are supported by the '536, which states “[e]xamples of excipients that can be used in the compositions formulated for oral administration are provided herein and can include... disintegrating agents, [and] lubricants.” EX1002, ¶199.

**Substitute Claim 69** narrows original claim 25’s recitation of the lubricants to only “ethyl laureate.” This amendment is responsive to and patentable over Grounds 6, which relies on Stegemann/HPE (Pet.66-67), by deleting the elements purportedly disclosed in Stegemann/HPE. **Support:** The '536 discloses “[l]ubricants that can be used in the pharmaceutical compositions...include... ethyl laureate...” EX1002, ¶206.

**Substitute Claim 70** narrows original claim 26’s recitation of “wherein the composition comprises from **0.01 mg** to 200 mg (Z)-endoxifen” to “wherein the composition comprises **20 mg** to 200 mg of (Z)-endoxifen,” and is responsive to and

patentable over Grounds 1-3. Petitioner relies on Ahmad's purported "teaching of a dosage between **1 and 10 mg/day**" (Ground 1), and Ahmad 2010's "dose of **4 mg**" and Ahmad 2012's "doses of **4.0-8.0 mg**" (Ground 3). Pet.32, 48-49. Critically, Ahmad, Ahmad 2010, and Ahmad 2012 all fail to disclose "wherein the composition comprises **20 mg to 200 mg** of (Z)-endoxifen." **Support:** The '536 discloses "[e]xamples of ranges for endoxifen in each dosage unit form are from 0.01 mg to 200 mg." EX1002, ¶263. The '536 repeatedly identifies the dose of 20 mg (*e.g.*, EX1002, ¶¶ 11, 18, 21) and further discloses "a composition comprising (Z)- endoxifen... wherein the composition is administered to the subject at a unit dose of...20 mg, 25 mg, 50 mg or 200 mg of (Z)-endoxifen." *Id.* ¶334; *see id.* ¶350.

**Substitute Claim 71** narrows original claim 27's recitation of "wherein the composition comprises from 1 mg to 20 mg of (Z)-endoxifen" to "wherein the composition comprises **20 mg** of (Z)-endoxifen," and is responsive to and patentable over Grounds 1-3. Petitioner relies on Ahmad's purported "teaching of a dosage between **1 and 10 mg/day**" (Ground 1), and Ahmad 2010's "dose of **4 mg**" and Ahmad 2012's "doses of **4.0-8.0 mg**" (Ground 3). Pet.32, 48-49. Critically, Ahmad, Ahmad 2010, and Ahmad 2012 all fail to disclose "wherein the composition comprises **20 mg** of (Z)-endoxifen." **Support:** The '536 states "the composition comprises about...20 mg of polymorphic Form III," and repeatedly identifies the specific dose

of 20 mg. EX1002, ¶178; *see also id.* ¶¶11, 13, 18, 21, 42, 44, 263, 292, 334-335, 350.

**Substitute Claim 72-73** are supported by the '536, which describes administering a “dose of a composition comprising 1 mg to 4 mg of (Z)-endoxifen.” EX1002, ¶¶223-224; *see id.* ¶263. The '536 further states “a composition comprising (Z)-endoxifen.... is administered to the subject at a unit dose of 1.0 mg, 1.5 mg, 2.0 mg, 4 mg,... [and] 8 mg.” *Id.* ¶350.

**Substitute Claim 74** is supported by the '536, which discloses “compositions” “*prepared in...fluid* unit dosage forms” (including “suspensions”). EX1002, ¶195. The '536 further states that the “composition...*further comprises* one or more excipient” and such “excipients that can be used in the compositions” can include “disintegrating agents” (e.g., “agar”), “lubricants” (e.g., “sorbitol”, “mannitol” “stearic acid,” “sodium lauryl sulfate”), “plasticizers” (e.g., “plant oils”), and “any combination thereof.” *Id.* ¶¶191, 199, 205-207, 212-213. Those disclosures convey possession of the recited suspension embodiments in which the suspension includes a fluid vehicle/excipient of the types expressly identified for fluid dosage forms. EX2030, ¶¶72-74. Petitioner itself asserts that “a suspension necessarily includes a fluid.” Pet.28.

**Substitute Claim 75** narrows original claim 31's recited fluids to a subset, and is responsive to and patentable over Grounds 1-2 and 5, which rely on Ahmad

and de Veilliers. Pet.29-30, 58-60. The amendment deletes the fluids purportedly disclosed in Ahmad and de Veilliers. **Support:** As discussed above for Substitute Claim 74, the '536 explains a suspension includes a fluid vehicle/excipient of the types expressly identified for fluid dosage forms. The '536 describes various excipients that can be used with the composition. *See* EX1002, ¶197 (“Accordingly, compositions designed for oral administration can be made with an inert or active excipient or with an edible carrier as disclosed herein.”). The '536 then describes that a lubricant can be used as an excipient. *Id.* ¶206. Thereafter, the '536 discloses that “[l]ubricants that can be used in the pharmaceutical compositions...include... sorbitol, mannitol,... stearic acid, sodium lauryl sulfate,... agar, and mixtures thereof.” *Id.* ¶206. Such lubricants serve as a suspension medium. *See id.* ¶¶191, 199, 205-207, 212-213; EX2030, ¶¶72-74; *see also* Substitute Claim 74.

**Substitute Claim 77** narrows original claim 33’s recitation of “administering **1 mg to 20 mg** of (Z)-endoxifen” to “administering **20 mg** of (Z)-endoxifen,” and is responsive to and patentable over Grounds 1-3. Petitioner relies on Ahmad’s purported “teaching of a dosage between **1 and 10 mg/day**” (Ground 1), and Ahmad 2010’s “dose of **4 mg**” and Ahmad 2012’s “doses of **4.0-8.0 mg**” (Ground 3). Pet.32, 48-49. Critically, Ahmad, Ahmad 2010, and Ahmad 2012 all fail to disclose “administering **20 mg** of (Z)-endoxifen.” **Support:** The '536 discloses that administering to a subject a dose of “20 mg of (Z)-endoxifen daily.” EX1002, ¶18. The '536

also repeatedly identifies the specific dose of 20 mg. *Id.* ¶178; *see also id.* ¶¶11, 13, 18, 21, 42, 44, 263, 292, 334-335, 350.

**Substitute Claims 78-79** are supported by the '536, which describes administering a “dose of a composition comprising 1 mg to 4 mg of (Z)-endoxifen.” EX1002, ¶223-24; *see id.* ¶263. The '536 further states “the present disclosure relates to a method of treating a subject in need thereof comprising administering a composition comprising (Z)-endoxifen or a salt or polymorph thereof prepared according to anyone of the processes disclosed herein, wherein the composition is administered to the subject at a unit dose of... 1.0 mg, 1.5 mg, 2.0 mg, 4 mg,... [and] 8 mg.” *Id.* ¶350.

**Substitute Claims 80-81** are supported by the '536, which states “administration of the oral composition comprising endoxifen or a salt or polymorph thereof maintains the subject’s plasma endoxifen at levels greater than 30 nM... at levels ranging from 30 nM to 300 nM (e.g., from 30 nM to 200 nM, or from 30 nM to 80 nM).” EX1002, ¶258; *see also id.* ¶248.

**Substitute Claim 82** amends original claim 38’s limitation from “releasing no more than **10%** of the (Z)-endoxifen in a stomach of the subject within **2** hours following the administering of the composition” to “releasing no more than **40%** of the (Z)-endoxifen in a stomach of the subject within **4** hours following the administering of the composition.” This is responsive to and patentable over Ground 7,

which relies on Cole to purportedly disclose “that its enteric coatings would not release any drug for **2 hours** in gastric fluid or in the stomach.” Pet.70-71. Critically, Cole’s disclosure is explicitly limited to a **2-hour** exposure, and Cole does not disclose or measure the amount of drug released in a stomach over a **4-hour** period. **Support:** The ’536 describes “wherein less than 40% of (Z)-endoxifen is released in the stomach after 4 hours of administration...as tested by a method of USP 711.” EX1002, ¶¶226, 227 (“a composition disclosed herein releases in the stomach...less than 40% of (Z)-endoxifen in 4 hours after administration...as tested by a method of USP 711.”), 303-304.

**Substitute Claim 83** amends original claim 39 from “releasing at least 50% of the (Z)-endoxifen in a small intestine of the subject **within** 8 hours...” to “**after** 8 hours...” This is responsive to and patentable over Ground 7, which relies on Ahmad in view of Cole to purportedly disclose the original requirement of “within” 8 hours. Critically, Cole does not disclose any data on release of a drug in intestinal fluid “after” 8 hours. **Support:** The ’536 states “the composition is formulated to release in the small intestine, such that... at least 50% of endoxifen is released after 8 hours after administration.” EX1002, ¶229.

**Substitute Claim 84** is supported by the ’536, which states “Area under Curve  $AUC_{(0-24hr)}$  (“ $AUC_{24hr}$ ”) describes the total exposure of the subject to a drug from time of dosing (0 hr) over a 24 hour period.  $AUC_{(0-inf)}$  (“ $AUC_{0-inf}$ ”), a time-

averaged concentration of drug circulating in the body fluid analyzed (normally plasma, blood or serum), describes the total exposure of the subject to a drug.... In some embodiments,  $AUC_{0-inf}$  ranges from 200 hr\*ng/mL to 10000 hr\*ng/mL.” EX1002, ¶270.

**Substitute Claim 85** is supported by the '536, which states: “Mean and individual (Z)-Endoxifen serum concentration-time curves were tabulated for each dose cohort.” EX1002, ¶468. Table 19C “Day 1 Model Pharmacokinetic Parameters by Treatment; Dose 4 mg” in column 2 for “Cmax (ng/mL)” lists a “Minimum” of “14.0” and “Maximum” of “62.0”. *Id.* ¶¶ 477, 479.

**Substitute Claim 86** is supported by the '536, which states “the composition is administered to a subject for the treatment or prevention of a hormone-dependent breast disorder, a hormone dependent reproductive tract disorder, or both in the subject.” EX1002, ¶14; *see also id.*, cls.37, 44, 47, 134.

**Substitute Claim 87** narrows original claim 43’s recited hormone-dependent breast disorder or hormone-dependent reproductive tract disorder to a subset, and is responsive to and patentable over Grounds 1-2, which rely on Ahmad to purportedly disclose benign breast disorder, hyperplasia, gynecomastia, and breast cancer. Pet.46. The amendment deletes the disorders purportedly disclosed in Ahmad. **Support:** The '536 discloses “compositions and methods for the treatment and/or prevention of hormone-dependent breast and reproductive tract (gynecologic)

disorders.” EX1002, ¶9. The ’536 describes that “[t]he hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder may be... increased breast density...DCIS, LCIS... precocious puberty, McCune-Albright Syndrome, endometrial cancer, ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, or vulvar cancer.” *Id.* ¶17; *see id.* ¶¶20, 39, 44, 239, 323, 329, 345, 361, 362-366, 372; cls.44-45, 55, 142, 157.

**Substitute Claim 88** is supported by the ’536, which states “[t]he subject may have tamoxifen-refractory or tamoxifen resistant hormone-dependent breast disorder or hormone-dependent reproductive tract disorder.” EX1002, ¶17.

## **VI. Conclusion**

For the foregoing reasons, if the Board finds any of original claims 1-44 unpatentable, the Board should grant this Motion and issue the corresponding proposed substitute claim(s) presented herein.

Respectfully Submitted by:  
/s/ Megan Raymond (Reg. No. 72,997)

Dated: January 26, 2026

**CERTIFICATE OF PAGE COUNT**

The undersigned certifies that the foregoing PATENT MOTION TO AMEND UNDER 37 C.F.R. § 42.221 INCLUDING REQUEST FOR PRELIMINARY GUIDANCE complies with the 25 page limit pursuant to § 42.24(a).

Dated: January 26, 2026

Respectfully Submitted,

By: /s/ Megan Raymond

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**CERTIFICATE OF SERVICE**

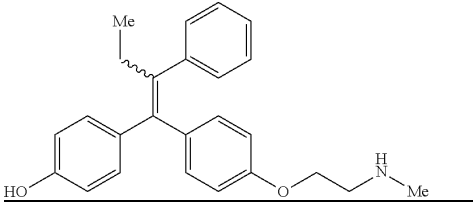
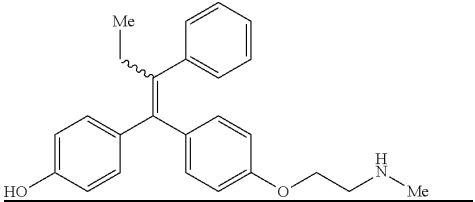
The undersigned hereby certifies that a copy of PATENT MOTION TO AMEND UNDER 37 C.F.R. § 42.221 INCLUDING REQUEST FOR PRELIMINARY GUIDANCE has been served in its entirety by causing the aforementioned document to be electronically mailed to the following attorneys of record for the Petitioner listed below:

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Dated: January 26, 2026

Respectfully submitted,  
By: /s/Sayem Osman/  
Sayem Osman

## APPENDIX A

Original Claim	Proposed Substitute Claim <sup>1</sup>
<p>1. A composition comprising an endoxifen and an enteric material, wherein: the endoxifen comprises a compound of Formula (III):</p> <p style="text-align: center;">Formula (III)</p>  <p>or a pharmaceutically acceptable salt thereof, and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>	<p><b>[1] 45.</b> A composition comprising an endoxifen and an enteric material, wherein: the endoxifen comprises a compound of Formula (III):</p> <p style="text-align: center;">Formula (III)</p>  <p>or a pharmaceutically acceptable salt thereof, <b><u>the endoxifen and the enteric material are mixed together,</u></b> and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>
<p>2. The composition of claim 1, wherein the pharmaceutically acceptable salt is selected from the group consisting of an: arecoline, besylate, bicarbonate, bitartrate, butylbromide, citrate, camysylate, gluconate, glutamate, glycollylarsanilate, hexylresorcinolate, hydrabamine, hydrobromide, hydrochloride, hydroxynaphthanoate, isethionate, malate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, pamaoate (Embonate), pantothenate, phosphate/diphosphate, polygalacuronate, salicylate, stearate,</p>	<p><b>[2] 46.</b> The composition of claim <b>[1] 45</b>, wherein the pharmaceutically acceptable salt is selected from the group consisting of an: arecoline, <b>[besylate,]</b> bicarbonate, <b>[bitartrate, butylbromide, citrate, camysylate, gluconate,]</b> glutamate, glycollylarsanilate, hexylresorcinolate, hydrabamine, <b>[hydrobromide, hydrochloride,]</b> hydroxynaphthanoate, isethionate, malate, mandelate, <b>[mesylate, methylbromide, methylnitrate,]</b> methylsulfate, mucate, <b>[napsylate, nitrate, pamaoate (Embonate),]</b> pantothenate, <b>[phosphate/diphosphate,]</b></p>

<sup>1</sup> Material that is added to the original claim by the proposed amendment is bolded and underlined. Material that is deleted from the original claim by the proposed amendment is bolded and bracketed.

## APPENDIX A

Original Claim	Proposed Substitute Claim <sup>1</sup>
sulfate, tannate, Teoclate, triethiodide, benzathine, clemizole, chlorprocaine, choline, diethylamine, diethanolamine, ethylenediamine, meglumine, piperazine, procaine, aluminum, barium, bismuth, lithium, magnesium, potassium, and zinc salt.	polygalacuronate, <b>[salicylate,]</b> stearate, <b>[sulfate,]</b> tannate, Teoclate, triethiodide, benzathine, clemizole, chlorprocaine, choline, diethylamine, diethanolamine, ethylenediamine, meglumine, piperazine, procaine, aluminum, barium, bismuth, lithium, magnesium, potassium, and zinc salt.
3. The composition of claim 1, wherein the pharmaceutically acceptable salt of the compound of Formula (III) is endoxifen gluconate.	<b>[3] 47.</b> The composition of claim <b>[1] 45</b> , wherein the pharmaceutically acceptable salt of the compound of Formula (III) is endoxifen gluconate.
4. The composition of claim 1, wherein the composition is a delayed-release formulation.	<b>[4] 48.</b> The composition of claim <b>[1] 45</b> , wherein the composition is a delayed-release formulation.
5. The composition of claim 1, wherein the composition is a tablet.	<b>[5] 49.</b> The composition of claim <b>[1] 45</b> , wherein the composition is <b><u>formulated as an uncoated</u></b> tablet.
6. The composition of claim 1, wherein the composition is a capsule.	<b>[6] 50.</b> The composition of claim <b>[1] 45</b> , wherein the composition is <b><u>contained within</u></b> a capsule.
7. The composition of claim 1, wherein the composition is uncoated.	<b>[7] 51.</b> The composition of claim <b>[1] 49</b> , wherein: <b><u>[the composition is uncoated]</u></b> <b><u>the composition comprises 20 mg of (Z)-endoxifen;</u></b> <b><u>the compound of Formula (III) is stable in the composition for at least 18 months at ambient temperature;</u></b> <b><u>and</u></b> <b><u>no more than 50% of the (Z)-endoxifen is released after 6 hours in gastric fluid, as measured in a dissolution test performed according to a method of USP 711.</u></b>

## APPENDIX A

Original Claim	Proposed Substitute Claim <sup>1</sup>
8. The composition of claim 1, wherein the composition comprises an enteric coating.	[8] <u>52</u> . The composition of claim [1] <u>45</u> , wherein the <b>enteric material [composition]</b> comprises an enteric coating.
9. The composition of claim 1, wherein the composition is formulated as a suspension.	[9] <u>53</u> . The composition of claim [1] <u>45</u> , wherein the composition is formulated as a suspension.
10. The composition of claim 9, wherein the suspension comprises a syrup or an elixir.	[10] <u>54</u> . The composition of claim [9] <u>53</u> , wherein the suspension comprises a syrup or an elixir.
11. The composition of claim 9, wherein the suspension comprises a fluid.	[11] <u>55</u> . The composition of claim [9] <u>53</u> , wherein the suspension comprises a fluid.
12. The composition of claim 11, wherein the fluid comprises an alcohol.	[12] <u>56</u> . The composition of claim [11] <u>55</u> , wherein the fluid comprises an alcohol.
13. The composition of claim 12, wherein the alcohol comprises ethanol.	[13] <u>57</u> . The composition of claim [12] <u>56</u> , wherein the alcohol comprises ethanol.
14. The composition of claim 9, wherein the suspension comprises an alcohol, a plant oil, a mineral oil, a glycol, an agar, or a mixture thereof.	[14] <u>58</u> . The composition of claim [9] <u>53</u> , wherein the suspension comprises <b>[an alcohol, a plant oil, a mineral oil, a glycol,] an agar[, or a mixture thereof]</b> .
15. The composition of claim 9, wherein the suspension comprises ethanol, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.	[15] <u>59</u> . The composition of claim [9] <u>53</u> , wherein the suspension comprises <b>[ethanol, mineral oil, glycerin,] sorbitol, mannitol, [polyethylene glycol, vegetable oil,] stearic acid, sodium lauryl sulfate, or a mixture thereof.</b>
16. The composition of claim 1, wherein the compound of Formula (III)	[16] <u>60</u> . The composition of claim [1] <u>45</u> , wherein the compound of Formula (III) is stable in the composition for at

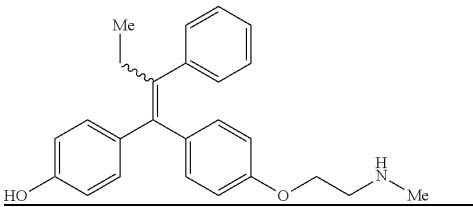
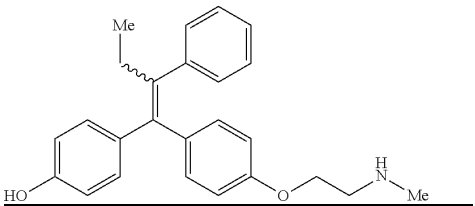
## APPENDIX A

Original Claim	Proposed Substitute Claim <sup>1</sup>
is stable in the composition for at least 10 days at about 25° C.	least <b>[10 days] 3 months</b> at about <b>[25°] 40°</b> C.
17. The composition of claim 1, formulated such that the composition is resistant to dissolution in an acidic environment for at least 2 hours, as measured in a dissolution test performed according to a method of USP 711.	<b>[17] 61.</b> The composition of claim <b>[1] 45</b> , formulated such that the composition is resistant to dissolution in an acidic environment for at least <b>[2] 4</b> hours, as measured in a dissolution test performed according to a method of USP 711.
18. The composition of claim 1, formulated such that the composition releases no more than 10% of the (Z)-endoxifen over 2 hours in gastric fluid, as measured in a dissolution test performed according to a method of USP 711.	<b>[18] 62.</b> The composition of claim <b>[1] 45</b> , formulated such that <b>[the composition releases]</b> no more than <b>[10%] 40%</b> of the (Z)-endoxifen <b>is released</b> over <b>[2] 4</b> hours in gastric fluid, as measured in a dissolution test performed according to a method of USP 711.
19. The composition of claim 1, formulated such that the composition releases at least 50% of the (Z)-endoxifen within 8 hours in intestinal fluid, as measured in a dissolution test performed according to a method of USP 711.	<b>[19] 63.</b> The composition of claim <b>[1] 45</b> , formulated such that <b>[the composition releases]</b> at least 50% of the (Z)-endoxifen <b>is released after [within]</b> 8 hours in intestinal fluid, as measured in a dissolution test performed according to a method of USP 711.
20. The composition of claim 1, wherein the composition further comprises hydroxypropylmethyl cellulose.	<b>[20] 64.</b> The composition of claim <b>[1] 45</b> , wherein the composition further comprises hydroxypropylmethyl cellulose.
21. The composition of claim 1, wherein the composition further comprises a filler.	<b>[21] 65.</b> The composition of claim <b>[1] 45</b> , wherein the composition further comprises a filler.
22. The composition of claim 21, wherein the filler comprises a sugar, salt, talc, calcium carbonate,	<b>[22] 66.</b> The composition of claim <b>[21] 65</b> , wherein the filler comprises a sugar, salt, talc, calcium carbonate,

## APPENDIX A

Original Claim	Proposed Substitute Claim <sup>1</sup>
microcrystalline cellulose, methyl cellulose, carboxymethyl cellulose, kaolin, mannitol, silicic acid, sorbitol, starch, pregelatinized starch, or combinations thereof.	microcrystalline cellulose, methyl cellulose, carboxymethyl cellulose, kaolin, mannitol, silicic acid, sorbitol, starch, pregelatinized starch, or combinations thereof.
23. The composition of claim 1, wherein the composition further comprises a disintegrant.	<b>[23] 67.</b> The composition of claim <b>[1] 45</b> , wherein the composition further comprises a disintegrant.
24. The composition of claim 1, wherein the composition further comprises a lubricant.	<b>[24] 68.</b> The composition of claim <b>[1] 45</b> , wherein the composition further comprises a lubricant.
25. The composition of claim 24, wherein the lubricant comprises calcium stearate, magnesium stearate, zinc stearate, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, stearic acid, sodium lauryl sulfate, talc, hydrogenated vegetable oil, ethyl oleate, ethyl laureate, agar, or combinations thereof.	<b>[25] 69.</b> The composition of claim <b>[24] 68</b> , wherein the lubricant comprises <b>[calcium stearate, magnesium stearate, zinc stearate, mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, stearic acid, sodium lauryl sulfate, talc, hydrogenated vegetable oil, ethyl oleate,] ethyl laureate[, agar, or combinations thereof]</b> .
26. The composition of claim 1, wherein the composition comprises from 0.01 mg to 200 mg (Z)-endoxifen.	<b>[26] 70.</b> The composition of claim <b>[1] 45</b> , wherein the composition comprises from <b>[0.01] 20</b> mg to 200 mg (Z)-endoxifen.
27. The composition of claim 1, wherein the composition comprises from 1 mg to 20 mg of (Z)-endoxifen.	<b>[27] 71.</b> The composition of claim <b>[1] 45</b> , wherein the composition comprises <b>[from 1 mg to] 20</b> mg of (Z)-endoxifen.
28. The composition of claim 1, wherein the composition comprises from 1 mg to 4 mg of (Z)-endoxifen.	<b>[28] 72.</b> The composition of claim <b>[1] 45</b> , wherein the composition comprises from 1 mg to 4 mg of (Z)-endoxifen.

**APPENDIX A**

Original Claim	Proposed Substitute Claim <sup>1</sup>
<p>29. The composition of claim 1, wherein the composition comprises 8 mg of (Z)-endoxifen.</p>	<p><b>[29] 73.</b> The composition of claim <b>[1] 45</b>, wherein the composition comprises 8 mg of (Z)-endoxifen.</p>
<p>30. A method of making the composition of claim 9, the method comprising suspending the endoxifen and the enteric material in a fluid.</p>	<p><b>[30] 74.</b> A method of making the composition of claim <b>[9] 53</b>, the method comprising suspending the endoxifen and the enteric material in a fluid.</p>
<p>31. The method of claim 30, wherein the fluid comprises an alcohol, ethanol, a plant oil, a mineral oil, a glycol, an agar, glycerin, sorbitol, mannitol, polyethylene glycol, vegetable oil, stearic acid, sodium lauryl sulfate, or a mixture thereof.</p>	<p><b>[31] 75.</b> The method of claim <b>[30] 74</b>, wherein the fluid comprises <b>[an alcohol, ethanol, a plant oil, a mineral oil, a glycol,] an agar, [glycerin,] sorbitol, mannitol, [polyethylene glycol, vegetable oil,] stearic acid, sodium lauryl sulfate, or a mixture thereof.</b></p>
<p>32. A method comprising administering to a subject a composition comprising an endoxifen and an enteric material, wherein: the endoxifen comprises a compound of Formula (III):</p> <div style="text-align: center;">  <p>Formula (III)</p> </div> <p>or a pharmaceutically acceptable salt thereof; and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>	<p><b>[32] 76.</b> A method comprising administering to a subject a composition comprising an endoxifen and an enteric material, wherein: the endoxifen comprises a compound of Formula (III):</p> <div style="text-align: center;">  <p>Formula (III)</p> </div> <p>or a pharmaceutically acceptable salt thereof; <b><u>the endoxifen and the enteric material are mixed together,</u></b> and at least 90% by weight of the compound of Formula (III) is (Z)-endoxifen.</p>

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33. The method of claim 32, comprising administering 1 mg to 20 mg of (Z)-endoxifen.	<b>[33] 77.</b> The method of claim <b>[32] 76</b> , comprising administering <b>[1 mg to]</b> 20 mg of (Z)-endoxifen.
34. The method of claim 32, comprising administering 1 mg to 4 mg of (Z)-endoxifen.	<b>[34] 78.</b> The method of claim <b>[32] 76</b> , comprising administering 1 mg to 4 mg of (Z)-endoxifen.
35. The method of claim 32, comprising administering 8 mg of (Z)-endoxifen.	<b>[35] 79.</b> The method of claim <b>[32] 76</b> , comprising administering 8 mg of (Z)-endoxifen.
36. The method of claim 32, wherein the administering of the composition maintains the subject's plasma endoxifen at a steady state level above 30 nM.	<b>[36] 80.</b> The method of claim <b>[32] 76</b> , wherein the administering of the composition maintains the subject's plasma endoxifen at a steady state level above 30 nM.
37. The method of claim 32, wherein the administering of the composition maintains the subject's plasma endoxifen at a steady state level from 30 nM to 300 nM.	<b>[37] 81.</b> The method of claim <b>[32] 76</b> , wherein the administering of the composition maintains the subject's plasma endoxifen at a steady state level from 30 nM to 300 nM.
38. The method of claim 32, further comprising releasing no more than 10% of the (Z)-endoxifen in a stomach of the subject within 2 hours following the administering of the composition.	<b>[38] 82.</b> The method of claim <b>[32] 76</b> , further comprising releasing no more than <b>[10%] 40%</b> of the (Z)-endoxifen in a stomach of the subject within <b>[2] 4</b> hours following the administering of the composition.
39. The method of claim 32, further comprising releasing at least 50% of the (Z)-endoxifen in a small intestine of the subject within 8 hours following the administering of the composition.	<b>[39] 83.</b> The method of claim <b>[32] 76</b> , further comprising releasing at least 50% of the (Z)-endoxifen in a small intestine of the subject <b>[within] after</b> 8 hours following the administering of the composition.
40. The method of claim 32, further comprising producing an area under curve (AUC <sub>0-inf</sub> ) of (Z)-endoxifen in the	<b>[40] 84.</b> The method of claim <b>[32] 76</b> , further comprising producing an area under curve (AUC <sub>0-inf</sub> ) of (Z)-

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subject of from 200 hr*ng/mL to 10,000 hr*ng/ml per 4 mg of (Z)-endoxifen administered.	endoxifen in the subject of from 200 hr*ng/mL to 10,000 hr*ng/ml per 4 mg of (Z)-endoxifen administered.
41. The method of claim 32, further comprising producing a maximum blood plasma concentration (C <sub>max</sub> ) of (Z)-endoxifen in the subject of from 14 ng/mL to 62 ng/ml per 4 mg of (Z)-endoxifen administered.	<b>[41] 85.</b> The method of claim <b>[32] 76</b> , further comprising producing a maximum blood plasma concentration (C <sub>max</sub> ) of (Z)-endoxifen in the subject of from 14 ng/mL to 62 ng/ml per 4 mg of (Z)-endoxifen administered.
42. The method of claim 32, further comprising treating a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder in the subject in need thereof.	<b>[42] 86.</b> The method of claim <b>[32] 76</b> , further comprising treating a hormone-dependent breast disorder or a hormone-dependent reproductive tract disorder in the subject in need thereof.
43. The method of claim 42, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is a benign breast disorder, hyperplasia, atypia, atypical ductal hyperplasia, atypical lobular hyperplasia, increased breast density, gynecomastia, ductal carcinoma in situ, lobular carcinoma in situ, breast cancer, precocious puberty, McCune-Albright Syndrome, endometrial cancer, ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, or vulvar cancer.	<b>[43] 87.</b> The method of claim <b>[42] 86</b> , wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is <b>[a benign breast disorder, hyperplasia, atypia, atypical ductal hyperplasia, atypical lobular hyperplasia,] increased breast density, [gynecomastia,] ductal carcinoma in situ, lobular carcinoma in situ, [breast cancer,] precocious puberty, McCune-Albright Syndrome, endometrial cancer, ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, or vulvar cancer.</b>
44. The method of claim 42, wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is tamoxifen-refractory or tamoxifen resistant.	<b>[44] 88.</b> The method of claim <b>[42] 86</b> , wherein the hormone-dependent breast disorder or the hormone-dependent reproductive tract disorder is tamoxifen-refractory or tamoxifen resistant.