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Paper 66
Date: July 16, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GALDERMA S.A.; GALDERMA LABORATORIES, INC.; GALDERMA LABORATORIES LP; GALDERMA RESEARCH & DEVELOPMENT SNC; NESTLÉ SKIN HEALTH, INC.; NESTLÉ SKIN HEALTH S.A.; and NESTLÉ S.A.,
Petitioner,

v.

MEDY-TOX, INC.,
Patent Owner.

PGR2019-00062
Patent 10,143,728 B2

Before ZHENYU YANG, CHRISTOPHER G. PAULRAJ, and TIMOTHY G. MAJORS, *Administrative Patent Judges.*

PAULRAJ, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Cancelling Original Claims 1–10
Denying Patent Owner's Non-Contingent Revised Motion to Amend With Regard to Proposed Substitute Claims 19–27
35 U.S.C. § 328(a)

I. INTRODUCTION

This is our Final Written Decision pursuant to 35 U.S.C. § 328(a). For the reasons discussed below, we hereby deny Patent Owner's non-contingent revised Motion to Amend with regard to proposed substitute claims 19–27. Paper 30 ("revised MTA" or "Rev. Mot."). We do not address the patentability of original claims 1–10, each of which is cancelled by virtue of the non-contingent revised MTA.

A. Procedural Background and Summary

Galderma S.A., et al., ("Petitioner") filed a Petition requesting post-grant review of claims 1–10 of U.S. Patent No. 10,143,728 B2 (Ex. 1001, "the '728 patent"). Paper 2 ("Pet."). Medy-Tox, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 11.

We determined that the '728 patent was eligible for post-grant review and that Petitioner demonstrated that it is more likely than not that at least one of the challenged claims was unpatentable. Accordingly, we instituted trial as to claims 1–10 of the '728 patent. Paper 14 ("Institution Decision" or "Dec.").

Following institution, Patent Owner did not file a Response to the Petition to contest the unpatentability arguments presented in the Petition with regard to the original claims, and instead chose to file a non-contingent Motion to Amend. Paper 21. In its Motion to Amend, Patent Owner requested that we provide Preliminary Guidance concerning the Motion to Amend in accordance with the Board's pilot program concerning motion to amend practice and procedures. Mot. 3; *see also* Notice Regarding a New Pilot Program Concerning Motion to Amend Practice and Procedures in Trial Proceedings Under the America Invents Act Before the Patent Trial and Appeal Board, 84 Fed. Reg. 9,497 (Mar. 15, 2019) (providing a patent

owner with the option to receive preliminary guidance from the Board on its motion to amend) ("Notice"). Petitioner filed an Opposition to the Motion to Amend. Paper 26.

In response to Patent Owner's request, we issued our Preliminary Guidance, indicating our initial, preliminary, non-binding views on whether Patent Owner had shown a reasonable likelihood that it had satisfied the statutory and regulatory requirements associated with filing a motion to amend in a post-grant review and whether Petitioner had established a reasonable likelihood that the substitute claims are unpatentable. Paper 28 ("Prelim. Guid.); *see* 35 U.S.C. § 326(d); 37 C.F.R. § 42.221; *see also* Notice, 84 Fed. Reg. at 9,497 ("The preliminary guidance . . . provides preliminary, non binding guidance from the Board to the parties about the [motion to amend].")

Patent Owner thereafter filed the non-contingent revised MMTA seeking to expressly cancel original claim 6 and replace the other original claims with proposed substitute claims 19–27. *See generally* Rev. Mot. Petitioner filed an Opposition to the revised MTA. Paper 40 ("Opp."). Patent Owner filed a Reply in support of its revised MTA, Paper 55 ("Reply"),[1] and Petitioner filed a Sur-Reply in opposition to the revised MTA, Paper 60.

After Patent Owner filed its revised MTA, the Chief Administrative Patent Judge extended the time to complete this proceeding by six months for good cause. Papers 32, 33, 34, 35. Prior to the oral hearing, we notified the parties of a potential *sua sponte* ground of unpatentability for substitute

[1] This corrected Reply replaced Patent Owner's originally filed Reply, Paper 52.

independent claim 19 as proposed in the revised MTA. Paper 54; *see Nike, Inc. v. Adidas AG*, 955 F.3d 45, 51 (Fed. Cir. 2020) (holding that the Board may *sua sponte* identify a patentability issue for a proposed substitute claim); *Hunting Titan, Inc. v. DynaEnergetics Europe GmbH*, IPR2018-00600, Paper 67 at 13 (PTAB July 6, 2020) (precedential) (explaining that the Board may, in rare circumstances, raise a ground of unpatentability not raised by the parties). We held the oral hearing on March 19, 2021, and the transcript of that hearing has been entered into the record. Paper 65 ("Tr.").

B. Real Parties-in-Interest

Petitioner initially identified Galderma S.A., Galderma Laboratories, Inc., Galderma Laboratories LP, Galderma Research & Development SNC, Nestlé Skin Health, Inc., Nestlé Skin Health S.A., and Nestlé S.A. as the real parties-in-interest for Petitioner. Pet. 4–5. Petitioner later updated its mandatory notices to indicate that Nestlé Skin Health S.A. was acquired by EQT Partners on October 2, 2019, and that Nestlé S.A. sold Galderma S.A., Galderma Laboratories, Inc., Galderma Laboratories L.P., Galderma Research & Development SNC, Nestlé Skin Health, Inc. (now SHDS, Inc.), and Nestlé Skin Health S.A. to an investment consortium of the following: (i) EQT Partners AB; (ii) PSP Investments; and (iii) Luxinva, a wholly owned subsidiary of Abu Dhabi Investment Authority. Paper 4. Petitioner contends that the consortium of investment partners are not real parties-in-interest because they did not have any role in directing, preparing, or filing the Petition, or any role in directing or controlling this proceeding. *Id.*

Patent Owner identifies Medy-Tox, Inc., Allergan Pharmaceuticals Ireland, Allergan Pharmaceuticals Holding (Ireland), and Allergan, Inc., as the real parties-in-interest for Patent Owner. Paper 5.

The parties do not dispute the identification of the real parties-in-interest.

C. Related Matters

Petitioner and Patent Owner report that the '728 patent is not the subject of any other judicial or administrative matter. Pet. 5; Paper 5, 2.

D. The '728 Patent

The '728 patent, titled "Long Lasting Effect of New Botulinum Toxin Formulation," discloses the use of an animal-protein-free botulinum toxin composition that exhibits a longer lasting effect compared to an animal-protein-containing botulinum toxin composition. Ex. 1001, codes (54), (57). The patent issued from an application (No. 15/336,119) filed October 27, 2016, but claims earliest priority to a provisional application (No. 61/915,476) filed December 12, 2013. *Id.* at codes (60), (63).

The specification explains that commercially available botulinum toxin A (BoNT/A) compositions, including BOTOX® (ona-BoNT/A), all contain animal proteins such as albumin and have a duration effect of approximately 3 months for treating conditions such as crow's feet lines or glabellar lines. *Id.* at 1:40–44. In contrast, the '728 patent claims methods of "locally administering a therapeutically effective amount of a botulinum toxin composition that does not comprise an animal-derived product or recombinant human albumin." *Id.* at 32:4–7.

As noted in the specification, animal-protein-free botulinum toxin compositions were previously disclosed in the inventors' prior patent applications, U.S. Application Publication No. 2010/0291136, now U.S. Patent No. 8,617,568 ("Jung I") (Exhibit 1006), and PCT/KR10–2012–0112248 ("Jung II") (Exhibit 1007), which are both incorporated by

reference in their entirety into the '728 patent. *Id.* at 2:63–3:20.[2] The specification notes that the use of polysorbate 20, methionine, and optionally isoleucine, instead of an animal-derived protein such as albumin or gelatin, as stabilizers for botulinum toxin eliminates the potential risk of infecting the recipient with serum-derived pathogens or microorganisms. *Id.* at 6:4–9. Furthermore, the specification indicates that an animal-protein-free botulinum toxin composition exhibits a longer lasting effectiveness compared to an animal-protein-containing botulinum toxin composition. *Id.* at 5:47–56.

In support of its conclusion regarding longer lasting efficacy, the specification describes the results of two clinical trials comparing an animal-protein-free botulinum toxin composition with botulinum toxin stabilized with human serum albumin. *See id.* at 13:60–31:55. Example 1 describes a Phase III clinical study that compared the efficacy of 20 units (U) liquid BoNTA/A (MT10109L), an animal-protein-free botulinum toxin composition, to 20 U BOTOX® in managing moderate to severe glabellar frown lines. *Id.* at 13:60–22:67. The specification indicates that the results presented from the Phase III study "demonstrate that MT10109L is not inferior to ona-BoNT/A in the improvement of glabellar lines and is relatively similar in safety," and "[w]ith its longer maintaining period of the glabellar line improvement, convenience without the additional dilution step, easy storage and re-usage, and animal derived protein-free constituents,

[2] Petitioner relies upon Jung I and Jung II for its anticipation and obviousness challenges presented in the Petition. Pet. 36–87. Petitioner does not, however, argue in this proceeding that the proposed substitute claims are anticipated or obvious. *See generally* Opp.

MT10109L is a desirable substitute for the conventional powder formulation of BoNT/A." *Id.* at 22:58–67.

Example 2 describes a Phase II clinical study that compared the efficacy of a lyophilized formulation of MT10109 versus BOTOX®, both administered at a 20 U dose. *Id.* at 23:1–31:55. Based on the data from the Phase II study, the specification concludes that "lyophilized MT10109 dosed at 20 U demonstrates similarity to BOTOX® at early time points (e.g. day 30)," and "[f]urther, it is demonstrated that MT10109 dosed at 20 U displays an increased sustained effect compared to BOTOX®, as the response of treatment was seen to be increased in the MT10109 20 U group compared to BOTOX® 20 U group at 120 days post treatment." *Id.* at 31:48–55.

E. Originally Challenged Claims and Asserted Grounds in Petition

Petitioner originally challenged claims 1–10 of the '728 patent, of which claim 1 is the only independent claim. In the Petition, Petitioner advanced five grounds of unpatentability in relation to these original claims. *See* Pet. 1. The grounds are summarized in the table below:

Claims Challenged	**35 U.S.C. §**	**Reference(s)/Basis**
1–10	112	Indefiniteness
1–10	112	Written Description
1–10	112	Enablement
1–3, 8	102	Jung I
1–8, 10	103	Jung I, Jung II, Allergan (ELN 1145), *BOTOX® COSMETIC (Botulinum Toxin Type A)* (2002) ("2002 Label")

In view of Patent Owner's election to file a non-contingent motion to amend, none of the originally challenged claims remain at issue in this proceeding. In particular, Patent Owner's non-contingent revised MTA expressly requests that we cancel original claim 6 and replace the remaining claims with revised substitute claims 19–27. Rev. Mot. 1. Although not expressly requested to be cancelled, we hereby also cancel original claims 1–5 and 7–10 because a non-contingent MTA is one in which "the Board provides a final decision on the patentability of substitute claims *in place of* determining the patentability of corresponding original claims." *See* Notice, 84 Fed. Reg. at 9,505 (emphasis added). Accordingly, we do not address the patentability of original claims 1–10 in this Final Written Decision insofar as all those claims are deemed cancelled by virtue of the non-contingent revised MTA and only address the patentability of proposed substitute claims 19–27.

II. ANALYSIS FOR MOTION TO AMEND

A. Legal Standards for Motions to Amend

In a post-grant review, amended claims are not added to a patent as of right, but rather must be proposed as part of a motion to amend. 35 U.S.C. § 326(d). The Board must assess the patentability of the proposed substitute claims "without placing the burden of persuasion on the patent owner." *See Aqua Prods., Inc. v. Matal*, 872 F.3d 1290, 1328 (Fed. Cir. 2017) (en banc); *see also Lectrosonics, Inc. v. Zaxcom, Inc.*, IPR2018-01129, Paper 15 at 3–4 (PTAB Feb. 25, 2019) (precedential). Ordinarily, "the petitioner bears the burden of proving that the proposed amended claims are unpatentable by a preponderance of the evidence." *Bosch Auto. Serv. Sols., LLC v. Matal*, 878 F.3d 1027, 1040 (Fed. Cir. 2017) (as amended on rehearing); *see also Lectrosonics*, Paper 15 at 3–4.

In determining whether a petitioner has proven unpatentability of the proposed substitute claims, the Board focuses on "arguments and theories raised by the petitioner in its petition or opposition to the motion to amend." *Nike*, 955 F.3d at 51. The Board itself also may justify any finding of unpatentability by reference to evidence of record in the proceeding. *Lectrosonics*, Paper 15 at 4 (citing *Aqua Products*, 872 F.3d at 1311 (O'Malley, J.)). "[O]nly under rare circumstances should the need arise for the Board to advance grounds of unpatentability to address proposed substitute claims that the petitioner did not advance, or insufficiently developed, in its opposition to the motion." *Hunting Titan*, Paper 67 at 9.

Before reaching the patentability issues that Petitioner argues, however, we first consider whether Patent Owner's revised MTA meets the statutory and regulatory requirements of 35 U.S.C. § 316(d) and 37 C.F.R. § 42.121. *Lectrosonics*, Paper 15 at 4. Patent Owner bears the burden of meeting these statutory and regulatory requirements. *See* "Guidance on Motions to Amend in view of *Aqua Products*" (2017), available at https://www.uspto.gov/sites/default/files/documents/guidance_on_motions_to_amend_11_2017.pdf. Accordingly, Patent Owner must demonstrate that: (1) the amendment proposes a reasonable number of substitute claims; (2) the amendment does not seek to enlarge the scope of the claims of the patent or introduce new subject matter; (3) the amendment responds to a ground of unpatentability involved in the trial; and (4) the original disclosure sets forth written description support for each proposed claim. *See* 35 U.S.C. § 326(d); 37 C.F.R. § 42.221.

B. Proposed Substitute Claims

In its revised MTA, Patent Owner requests that we cancel original claim 6 and replace original claims 1–5 and 7–10 with revised substitute

claims 19–27. Rev. Mot. 1–2. Proposed substitute claim 19, which would replace claim 1, recites (with underlining and strikethroughs representing, respectively, text added to and deleted from claim 1, and added bracketed letters (e.g., [a], [b], etc.) correlating to Patent Owner's indication of specific claim limitations):

> 19. A method for treating glabellar lines ~~a condition~~ in a patient in need thereof, comprising:
>
> [a] locally administering a first treatment of ~~therapeutically effective amount of~~ a botulinum toxin composition comprising a serotype A botulinum toxin in an amount present in about 20 units of MT10109L, a first stabilizer comprising a polysorbate, and at least one additional stabilizer, and that does not comprise an animal-derived product or recombinant human albumin;
>
> [b] locally administering a second treatment of the botulinum toxin composition at a time interval after the first treatment;
>
> [c] wherein said time interval is the length of effect of the botulinum toxin composition as determined by physician's live assessment at maximum frown;
>
> [d] wherein said botulinum toxin composition has a greater length of effect compared to about 20 units of BOTOX®, when ~~whereby the botulinum toxin composition exhibits a longer lasting effect in the patient when compared to treatment of the same condition with a botulinum toxin composition that contains an animal-derived product or recombinant human albumin dosed at a comparable amount and~~ administered in the same manner for the treatment of glabellar lines ~~and to the same location(s)~~ as that of the botulinum toxin composition; and
>
> [e] wherein said greater length of effect is determined by physician's live assessment at maximum frown and

> requires a responder rate at 16 weeks after the first treatment of 50% or greater. ~~that does not comprise an animal-derived product or recombinant human albumin, wherein the condition is selected from the group consisting of glabellar lines, marionette lines, brow furrows, lateral canthal lines, and any combination thereof.~~

C. Level of Ordinary Skill in the Art

In the Petition, Petitioner proposes that a person of ordinary skill in the art ("POSA") "would have an advanced degree in biochemistry or molecular biology with at least 5 years of experience in formulations involving botulinum toxin and clinical studies involving such formulations." Pet. 10 (citing Ex. 1004 ¶ 14).

Patent Owner asserts that a POSA for the '728 patent should include:

> A person having a medical degree who practices dermatology, aesthetic medicine, cosmetic surgery or other related disciplines, and has been trained in and has experience with administering botulinum toxin injections, including at least five years of experience with injecting botulinum toxin formulations and evaluating results of those treatments in patients or a person with an advanced degree in biochemistry, molecular biology or other related discipline with at least 5 years of experience in protein compositions, such as botulinum toxins, and/or clinical studies involving such compositions.

Rev. Mot. 2 (citing Ex. 2032 ¶ 62).

Patent Owner contends that the definition of a POSA must include physicians "because the claims are primarily directed to physicians, whom utilize the claimed methods of treatment, and have the most knowledge regarding the prior art." *Id.* Patent Owner notes that its expert Dr. Singh is a physician "who has years of experience in administering neurotoxins [and] understands the clinical significance of the claims and prior art," whereas

"Petitioner's expert, Dr. Ramzan, is not a physician and has never treated any patients with such toxins." *Id.* at 2–3.

In our Institution Decision, we determined, based on the record at the time, that a POSA would encompass the definition asserted by Petitioner. Dec. 8. We maintain that determination based on the full evidence of record adduced in this proceeding.

Factors that may be considered in determining level of ordinary skill in the art include: (1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field. *Orthopedic Equip. Co. v. All Orthopedic Appliances, Inc.*, 707 F.2d 1376 at 1381–82 (Fed. Cir. 1983).

We recognize that the claims are directed to methods of treatment, and agree that a "clinician" or a "physician" may indeed have some relevant experience implementing the claimed methods. But we are not persuaded that the POSA must necessarily have a medical degree (M.D.) or be a medical doctor to the extent that Patent Owner seeks to impose such requirements on the POSA. In this regard, we note that none of the inventors are physicians themselves. *See* Ex. 1059 ¶ 7 (recounting that inventors Chang-Hoon Rhee and Gi-Hyeok Yang have PhDs, and inventor Hyun Jee Kim has a Master's degree in Pharmacy); Ex. 1050, 1; Ex. 1051, 1; Ex. 1052, 3. And although some of the publications of record appear to be authored by individuals with medical degrees, we do not find that the record suggests that being a physician is a prerequisite to working in the field of botulinum toxins relevant to the claims. As such, even though Petitioner's expert, Dr. Ramzan, does not have a medical degree, we find

that he is qualified to provide an opinion from the perspective of a POSA in this proceeding based on his education and prior work experience in the field and credit his testimony accordingly. *See* Ex. 1004 ¶ 5 (identifying experience working on *C. botulinum* toxins, including work on "approximately 6 products at various stages of clinical and commercial development in the United States, Europe, and South Korea").

D. Claim Construction

We interpret a claim "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b)." 37 C.F.R. § 42.100(b) (2019). This standard requires that we construe claims "in accordance with the ordinary and customary meaning of such claim[s] as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *Id.*

Patent Owner did not propose any claim constructions for the substitute claims in its revised Motion. In its Opposition to the revised Motion, Petitioner contends that "[t]he term '***a serotype A botulinum toxin***' should be construed to mean 'any serotype A botulinum neurotoxin,' irrespective of whether it is in complexed or purified form and irrespective of the size of the complex." Opp. 1. Petitioner relies upon the definition for "botulinum toxin" set forth in the '728 patent as "a botulinum neurotoxin as either pure toxin or complex, native, recombinant, or modified, and includes botulinum toxin type A[.]" *Id.* (citing Ex. 1001, 4:21–23). Thus, Petitioner contends that "the substitute claims encompass any serotype A botulinum neurotoxin, including the 900 kDa complex known as onabotulinumtoxinA, the mixture of 600 and 300 kDa complexes known as abobotulinumtoxinA, and the purified, uncomplexed 150 kDa toxin known as incobotulinumtoxinA." *Id.* (citing Ex. 1094, 14:3–15). Patent Owner

responds that "no construction is necessary as this term has a plain and ordinary meaning that a POSA would understand, which both parties have previously acknowledged." Reply 1.

Upon review of the parties' contentions, we determine that we need not expressly construe "serotype A botulinum toxin" to resolve any disputed issues of patentability for the proposed substitute claims. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("[O]nly those terms need to be construed that are in controversy, and only to the extent necessary to resolve the controversy."); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (applying *Vivid Techs.* in the context of an *inter partes* review).

The parties also dispute whether the limitation requiring a responder rate of "50 or greater" should be interpreted as a range of 50–100% (as argued by Petitioner) or merely a minimum threshold of 50% (as argued by Patent Owner). We address this issue as part of our analysis below.

E. Statutory and Regulatory Requirements

1. Reasonable Number of Substitute Claims

"There is a rebuttable presumption that a reasonable number of substitute claims per challenged claim is one (1) substitute claim." *Lectrosonics*, Paper 15 at 4–5; 37 C.F.R. § 42.221(a)(3). Here, Patent Owner's revised MTA proposes nine substitute claims for nine of the originally challenged claims. *See* Rev. Mot., App'x A. Thus, the revised MTA complies with the requirement that the amendment propose a reasonable number of substitute claims.

2. Responsive to Ground of Unpatentability

Patent Owner's revised MTA responds to a ground of unpatentability involved in this trial. *See* 37 C.F.R. § 42.221(a)(2)(i). In particular, Patent

Owner's claim amendments add features in an attempt to distinguish the proposed substitute claims from the references as well as to address one or more of the § 112 grounds asserted by Petitioner and/or addressed in our Preliminary Guidance. Rev. Mot. 10–11; *see* Notice, 84 Fed. Reg. at 9,501 ("A revised MTA must provide amendments, arguments, and/or evidence in a manner that is responsive to issues raised in the preliminary guidance (if requested) or the petitioner's opposition to the MTA.").

3. No Enlargement of Claim Scope

"A motion to amend may not present substitute claims that enlarge the scope of the claims of the challenged patent." *Lectrosonics*, Paper 15 at 6–7; 35 U.S.C. § 326(d)(3); 37 C.F.R. § 41.221(a)(2)(ii).

Petitioner argues that proposed substitute claims 19 and 21–27 improperly broaden the claims beyond the original scope by eliminating the phrase "dosed at a comparable amount" and introducing two new requirements, namely that the botulinum toxin composition (1) contains the same amount of neurotoxin as in about 20U MT10109L and (2) has a greater length of effect compared to about 20U of BOTOX® (claim 19[a], [d]). Opp. 2.

Petitioner contends that the "'dosed at a comparable amount' limitation in the original claims refers to a unit dose," whereas "the substitute claims have been rewritten to require the botulinum toxin be administered in the same amount by weight of neurotoxin as is in 20U of MT10109L, eliminating comparable unit doses and fundamentally transforming the substitute claims." *Id.* at 3–4.

To illustrate this point, Dr. Ramzan provides a comparison of three botulinum neurotoxin products that were commercially available in the U.S. (*i.e.*, BOTOX®, DYSPORT®, and XEOMIN®). Ex. 1106 ¶¶ 31–38. Based

on dose equivalency studies, Dr. Ramzan indicates that comparable unit doses between the products are 50U of DYSPORT® to 20U of BOTOX® and 20U of XEOMIN® to 20U of BOTOX®. *Id.* ¶ 27. And based on published data from a peer-reviewed scientific journal measuring the mass of 150 kDa neurotoxin in each of the products and an assumption that 20U of MT10109L contains 0.17 ng of the 150 kDa neurotoxin protein, Dr. Ramzan asserts that "to administer 0.17 ng of the neurotoxin in XEOMIN®, one would need to inject 39U into a patient (or 0.17 ng multiplied by 100U/0.44 ng)." *Id.* ¶ 34. Thus, Dr. Ramzan opines, the 39U derived applying a "by weight" calculation (like allegedly required in the substitute claims) "is significantly higher than 20U of XEOMIN®, the dose equivalent of 20U of BOTOX®" (like allegedly required applying the original claim language). *Id.* Likewise, Dr. Ramzan asserts that "to administer 0.17 ng of DYSPORT®, one would need to inject 26U into the patient (or 0.17 ng multiplied by 100U/0.65," which "is significantly lower than 50U of DYSPORT®, the dose equivalent of 20U of BOTOX®." *Id.* Dr. Ramzan summarizes the comparison in the following chart:

Product	Comparable Dose to 20U of BOTOX® By Clinical Equivalence	Unit Dose Required to Administer the Same Amount By Weight of Neurotoxin in 20U of MT10109L	Δ
XEOMIN®	20U	39U	+19U (+95%)
DYSPORT®	50U	26U	-24U (-48%)

Chart comparing "Comparable Dose" and "Same Amount By Weight" for the products XEOMIN® and DYSPORT®

The chart above indicates a +19U (+95%) dosing variance for XEOMIN® and a -24U (-48%) dosing variance for DYSPORT® depending on whether a "Comparable Dose" or "By Weight" methodology is used. According to Petitioner and Dr. Ramzan, the large variances in the chart above show that "there is no correlation between (i) the dose required to administer the same amount by weight of neurotoxin in 20U of MT10109L and (ii) the equivalent dose to 20U of BOTOX®." *Id.* ¶ 35; Opp. 5–6.

Patent Owner responds that the amendment to remove the "dosed at a comparable amount" was to address the Board's concerns in the Preliminary Guidance that the claims lack written description support in view of the fact that the claims are not limited to administration of a 20 Units dose. Reply 2. Patent Owner also contends that the amendment also addressed Petitioner's prior argument that "comparable amount" broadly covered "***any*** animal protein-free composition when dosed at ***any*** comparable amount of ***any*** animal-protein containing composition." *Id.* at 2–3. According to Patent Owner, the claims now recite botulinum toxin compositions comprising a specific amount—the amount of toxin present in about 20 units of MT10109L—which is not broader than "any comparable amount." *Id.* at 3.

We do not agree with Petitioner's argument that the proposed amendments are broader in scope than the original claims. Original claim 1 recites that "the botulinum toxin composition exhibits a longer lasting effect in the patient when compared to treatment of the same condition with a botulinum toxin composition that contains an animal-derived product or recombinant human albumin dosed at a comparable amount." Ex. 1001, 32:8–13. As noted by Petitioner, the comparison required by the original claims was based on unit doses of an animal protein-containing botulinum toxin composition and an animal-protein-free botulinum toxin composition

as determined using an LD_{50} assay. Opp. 3. This was problematic according to Petitioner insofar as each manufacturer uses its own proprietary LD_{50} assay, and thus there was no uniform method by which those skilled in the art could make the required comparison. *Id.* Proposed substitute claim 19 now removes this ambiguity by reciting a composition with serotype A botulinum toxin in an amount present in about 20 units of MT10109L, and requiring a comparison of the length of effect of such a composition with 20 units of BOTOX®.

Although the basis for the comparison has shifted from unit doses to weight, we do not agree with Petitioner's argument that this amendment improperly broadens the claims' scope. To the contrary, based on the record here, Patent Owner persuades us that the amendment in question now indicates a more specific amount of neurotoxin that falls within the scope of the original claims—addressing Petitioner's past criticisms and responding to our concerns about unit dosing language of the earlier claims as explained in the Preliminary Guidance. *See* Prelim. Guid. 6–7; Ex. 2072 ¶ 19 (noting 1 ng of a 900 kDa toxin complex, which includes the 150kDa toxin); Ex. 1106 ¶ 34 (noting a 0.17 ng weight for the 150kDa serotype A toxin protein); Tr. 42:22–48:17 (discussing calculations to arrive at 0.17–0.18 nanograms of the serotype A toxin). We find no sufficient and persuasive evidence of record suggesting that the proposed substitute claims encompass a larger number of compositions than the original claims.

Accordingly, we determine that the scope of each of the proposed substitute claims is not improperly broader than the claim for which it is a substitute.

4. No New Matter

"A motion to amend may not present substitute claims that . . . introduce new subject matter." *Lectrosonics*, Paper 15 at 6–7; 35 U.S.C. § 326(d)(3); 37 C.F.R. § 41.221(a)(2)(ii). To evaluate compliance with the prohibition on amendments that add new matter,

> the Board requires that a motion to amend set forth written description support in the originally filed disclosure of the subject patent for each proposed substitute claim, and also set forth support in an earlier filed disclosure for each claim for which benefit of the filing date of the earlier filed disclosure is sought.

Lectrosonics, Paper 15 at 7.

The revised MTA provides a chart listing purported written description support in the originally filed disclosures of U.S. Patent Application No. 15/336,119 ("the '119 application"), U.S. Patent Application 14/567,289, and Provisional U.S. Patent Application No. 61/915,476 for each of the proposed substitute claim limitations. Rev. Mot. 5–7.

Petitioner contends that proposed substitute claims 19–27 introduce new matter by including the claimed "responder rate" limitation, i.e., the requirement that "wherein said greater length of effect requires a responder rate at 16 weeks after the first treatment of 50% or greater." Opp. 12–16. In its Opposition to the original Motion to Amend, Petitioner had previously argued that the 16-week responder rate should be interpreted as a range of 50–100%. Paper 26, 3. In its Opposition to the revised MTA, Petitioner now contends that this claim limitation lacks written description support even under Patent Owner's construction of "50% or greater" as requiring a minimum threshold, rather than a range up to 100%. Opp. 12. Although

Examples 1 and 2 in the '728 patent's specification provide 62% and 52% responder rates for two specific formulations, Petitioner contends that "unpredictability in the art would lead a POSA to conclude that the inventors were only in possession of formulations exhibiting those specific 16-week responder rates, not a minimum threshold of 50%." *Id.* at 13. According to Petitioner, Patent Owner "could have equally selected a minimum threshold of 45%, which would encompass the responder rates of Examples 1 and 2 and is greater than the 16-week responder rates for 20U of BOTOX® in both examples as originally defined in the specification," and thus Patent Owner is redefining how the specification expressly defines the "greater length of effect" by now writing a 50% minimum threshold 16-week responder rate requirement into the substitute claims. *Id.* at 14.

Petitioner further argues that there is no practical difference between Patent Owner's alleged "50% minimum threshold" construction and Petitioner's proposed range of "50-100%." *Id.* In support of this contention, Petitioner points to the deposition testimony of Patent Owner's expert Dr. Singh as acknowledging that compositions with 70%, 80%, and 90% responder rates all meet Patent Owner's minimum threshold of 50%. *Id.* (citing Ex. 1089, 34:23–36:17). Petitioner asserts that Dr. Singh confirmed that "it would be impossible to speculate . . . with any accuracy" how to modify any of the formulations in the '728 patent to achieve such higher responder rates. *Id.* (citing Ex. 1089, 30:2–31:1).

In its Reply in support of the revised MTA, Patent Owner argues that Petitioner mistakenly alleges that examples from the specification (showing 62% and 52% responder rates) are insufficient to support the 50% threshold limitation. Reply 7. Citing *In re Wertheim*, 541 F.2d 257, 263 (CCPA 1976), Patent Owner contends that these examples provide sufficient written

description support for the responder rate limitation because "there is no requirement for exact correspondence between claim language and disclosed embodiments." *Id.* Patent Owner also notes that "Dr. Singh explains that a 50% responder rate is clinically meaningful to a POSA, especially considering the use by others in the art of the 50% response rate to determine efficacy of botulinum toxin to treat glabellar lines." *Id.* (citing Ex. 2062 ¶¶ 20–23).

Based on the record developed in this proceeding, we find that the proposed substitute claims introduce new matter in the claimed "responder rate" limitation. We recognize that in our Preliminary Guidance, we noted based on the record at the time that we were not of the view that the limitation should necessarily be interpreted as a range of 50–100%. Prelim. Guide 5–6. However, the record has been further developed since we issued our Preliminary Guidance. As noted by Petitioner, Patent Owner's expert Dr. Singh acknowledged during his deposition (taken after our Preliminary Guidance issued) that the proposed substitute claims encompass responder rates as high as 90%. Ex. 1089, 34:23–36:17. Patent Owner's counsel similarly acknowledged during the oral hearing that the proposed substitute claims would read on higher responder rates, including up to 95%, but continued to take the position that the claim limitation was intended to impose only a minimum threshold of 50%. Tr. 62:6–20 (Patent Owner's counsel agreeing the claims encompass higher responder rates, such as 75%, 85%, and 95%); *see also id.* at 67:12–68:13 (Patent Owner's counsel stating that an interpretation of between 50–100% does not affect Patent Owner's argument). But even if the responder rate limitation was only intended to set a "floor" rather than a "ceiling," Patent Owner's counsel acknowledged that there will nonetheless be a natural upper limit of 100% for the claimed

responder rate. *Id.* at 64:2–6 ("I think that you can't have a responder rate over 100 percent. . . . You can't have more people respond than you have patients."); *see also id.* at 64:18–20 ("[I]nherently a person of skill in the art looking at the specification would know you can't exceed 100 percent."). An open-ended range would raise separate issues of indefiniteness and enablement under 35 U.S.C. § 112. *See* MPEP § 2173.05(c) (II) ("Open-ended numerical ranges should be carefully analyzed for definiteness.); *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1383 (2012) (determining that claim term "change in the resistance by at least 10%" lacked enablement because it was interpreted to be an open-ended range with no upper limit). As such, upon further consideration of the record, we adopt Petitioner's proposed construction and interpret the limitation requiring a responder rate of "50% or greater" as a range of 50–100%.

The test for determining compliance with the written description requirement is not simply the presence or absence of literal support in the specification for the claim language, but rather, whether the disclosure of the application as originally filed reasonably conveys to a person of ordinary skill in the art that the inventor had possession of the claimed subject matter at the time of filing. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991); *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983). It is well settled that the written description requirement of § 112 requires the disclosure to convey that Patent Owner had possession of the entire range. *In re Lukach*, 442 F.2d 967, 969 (CCPA 1971) (holding that a single disclosure of a value within a range does not provide support for the entire range).

It is undisputed that the phrase "50% or greater" does not appear in the specification of the '728 patent. Nonetheless, as purported written description support for the responder rate limitation, Patent Owner provides the following citations in the '119 application (Ex. 1003) that issued as the '728 patent and similar citations in the priority applications:

Citation	Description
8:7–3	Provides a general description of the invention, noting that "the animal-protein-free botulinum toxin composition exhibits a longer lasting effectiveness compared to an animal-protein-containing botulinum toxin composition" when the patient was evaluated at 16 weeks.
15:12–16:7	Describes the time between the first and second treatments of the animal-free botulinum toxin as ranging from one month up to 52 weeks or more; notes that "[i]n certain embodiments, the time between the first and second treatment . . . is greater than 16 weeks for the effective alleviation of at least one symptom."
19:25–31	Notes that "[i]n certain embodiments, in a treatment method of the invention, a therapeutically effective level botulinum toxin is present in the recipient patient for an extended period of time of at least 16 weeks" up to 50 weeks or more.
20:25–43:2	Broad citation to the Experimental Examples section (Examples 1 and 2).
22:7–11	Describes the 16-week study design for Example 1, noting that each subject received a 5 point intramuscular injection with a total dose of 20U of MT10109L or BOTOX®.
23:6–15	Describes the "primary efficacy end point" of the study as the percentage of responders at maximum frown at week 4 based on the investigator's live assessment (face-to-face observation). Further describes "secondary efficacy end point" to include: 1) percentage of responders at maximum frown at weeks 16; 2) percentage of responders of glabellar lines at rest based on investigator's 10 live assessment at weeks 4 and 16; and 3) percentage of responders at maximum frown and at rest based on photographic assessment at week 4. Notes that "[i]n accordance with previous studies for ona-BoNT/A, responders were defined

Citation	Description
	as those who have post-treatment [Facial Wrinkle Scale (FWS)] scores of 0 or 1 with pretreatment FWS scores of 2 or 3," and "[t]his means an improvement of at least 1 point for the subjects with moderate wrinkles and at least 2 points for the 15 subjects with severe wrinkles."
26:3–8	"The percentage of responders at maximum frown by live assessment at weeks 16 was significantly lower in ona-BoNT/A group than MT10109L group. The percentage of responders in PP set was 62.34% in MT10109L group and 40.51% in ona-BoNT/A group (p value = 0.0064) (Table 3). And the percentage of responders in FAS set was 60.71% in MT10109L group and 41.67% in ona-BoNT/A group (Table 3, Figure 3B). Both PP set and FAS set showed significant difference in two groups and superiority of MT10109L."
32:29–33:8	Describes the Phase II study of Example 1, noting that "[t]he results presented here compare the safety and efficacy of lyophilized formulation of MT10109 and BOTOX® in subjects with moderate to severe glabellar lines" and that it was "demonstrated that the response at maximum frown was sustained in the MT10109 20U group for up to 120 days." Notes that the experiments compared dosing of MT10109 at 10U, 20U and 30U to BOTOX® dosed at 20U Further notes that the efficacy was primarily assessed at Day 30 and "the comparison of interest was the comparison between the responder rates for MT10109 20 U and BOTOX® 20 U." "A responder was defined as a glabellar line severity rating of none (0) or mild (1) at maximum frown or at rest at Day 30, depending on the analysis."
36:14–37:4	"The proportion of responders at maximum frown decreased in all treatment groups from Day 14 to Day 120 (based on the investigator's live assessment). The proportions at Day 120 were greater in the MT10109 20 U group compared with BOTOX® 20 U and the other MT10109 groups (Figure 6)." "The proportion of responders at maximum frown in the MT 10109 20 U group at Day 60, and at Day 120 was 65.2% (15 of 23 subjects) and 52.2% (12 of 23 subjects), respectively, and in the BOTOX® 20 U group was 68.0%

Citation	Description
	(17 of 25 subjects) and 23.1 % (6 of 26 subjects), respectively (Table 9)."
Table 1	Identifies for Example 1 study "Scales to assess the effectiveness of MT10109L and Ona-BonT/A."
Table 3	Provides data from Example 1 study for "Responder rate by live assessment at maximum frown."
Table 9	Provides data from Example 2 study for "Investigator's Live Assessment Rating of Glabellar Line Severity at Other Visits, Full Analysis Set."

As indicted above, Patent Owner points to data included in the specification showing 16-week responder rates of 52%, 61%, and 62%, which are all greater than 50%. Ex. 1003, 26:3–8, 36:14–37:4. The issue is whether these discrete data points support the full claimed range of 50–100%. We find that it does not. The disclosure and data in the specification might support a method by which to achieve responder rates of 50% to about 62%, but this does not suggest—and the specification does not describe—that the inventors were capable of achieving significantly higher responder rates (up to 100%) using the MT10109L formulation. In this regard, we note that the specification recognizes that responder rate differences of about 20% between MT1019L and ona-BoNT/A were considered to be "significant." *Id.* at 26:7–8. A responder rate of, for example, 82%, although it is encompassed by the claims and would represent a "significant" result well beyond a 62% rate, is nowhere described in the specification. As such, there is no basis to conclude that the inventors were in possession of a method that could achieve a responder rate up to 38% higher than the highest responder rate described in the applications to which the '728 patent claims priority.

The *Wertheim* case does not support Patent Owner's position. In *Wertheim*, the court considered whether there was sufficient written description support in a foreign priority application for claim limitations reciting a coffee solid content of "at least 35%" and "between 35% and 60%." 541 F.2d at 261–62. The specification of the priority application indicated that ground roasted coffee is concentrated prior to foaming by suitable means "until a concentration of 25 to 60% solid matter is reached," while the examples disclosed embodiments having solids contents of 36% and 50%. *Id.* at 262. The court found that this disclosure did not provide written description support for the claims reciting "at least 35%" because that limitation "reads literally on embodiments employing solids contents outside the 25-60% range described in the Swiss application." *Id.* at 263. The court further noted that appellants did not meet their burden of showing that the upper limit of solids content described, i.e., 60%, is inherent in "at least 35%." *Id.* at 264. The court, however, found that the claims reciting a solid content range of "between 35% and 60%" presented a different question because that claimed range fell within the broader described range of 25% to 60% and was further supported by the specific example with a solid content of 36%. *Id.* The court noted that:

> In the context of this invention, in light of the description of the invention as employing solids contents within the range of 25-60% along with specific embodiments of 36% and 50%, we are of the opinion that, as a factual matter, persons skilled in the art would consider processes employing a 35-60% solids content range to be part of appellants' invention and would be led by the Swiss disclosure so to conclude.

Id. at 264.

We find that the written description issue in this case with respect to the "50% or greater" responder rate limitation is analogous to the written

description issue with respect to the "at least 35%" limitation addressed in *Wertheim*. Indeed, there appears to be even less written description support for the limitation here compared to *Wertheim* insofar as Patent Owner has not identified the disclosure of a narrower range in the specification to support the broader claimed responder rate range. Rather, Patent Owner has identified only discrete 16-week responder rates of 52%, 61%, and 62% from the examples, but we find that none of these examples would suggest to a POSA that the inventors were in possession of a method that achieves responder rates significantly higher than 62%, including up to 100%.

In *Wertheim*, the court also addressed a new matter rejection under 35 U.S.C. § 132 with respect to a claim limitation requiring that the frozen foam be ground "to a particle size of at least 0.25 mm." *Id.* at 265–66. As noted by the court, the new matter rejection was "tantamount to a rejection of the claims on the description requirement of 35 U.S.C. § 112, first paragraph." *Id.* at 265. Notwithstanding the specification's indication of a preferred particle size range of 0.25 to 2 mm, the court found that the "at least 0.25 mm" limitation (with no upper limit) was supported by an alternative embodiment disclosed in the specification in which freeze-dried plates or lumps are subsequently ground to the desired particle size. *Id.* at 265–66. The court held that "[t]he clear implication of this disclosed modification is that appellants' specification does describe as their invention processes in which particle size is 'at least 0.25 mm,' without upper limit, as delineated by the rejected claims." *Id.* at 266. As such, because the inventive aspect of the limitation at issue in that case related to achieving *smaller* particle sizes for the ground coffee, the court was not concerned with the fact that there was no upper limit for the "at least 0.25 mm" particle size claim limitation. We find this to be distinguishable from the "50% or

greater" limitation at issue in this proceeding. In this case, there is no indication in the specification that the inventors of the '728 patent contemplated achieving responder rates up to 100%. But even if that were considered an implicit goal, the specification does not suggest that the inventors were in possession of a method that would have achieved such higher rates using the claimed animal-protein-free botulinum toxin compositions. *Cf. AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1300 (Fed. Cir. 2014) (holding insufficient a disclosure that is "only a research plan, leaving it to others to explore the unknown contours of the claimed genus").

In sum, for the foregoing reasons, we find that the inclusion of the "50% or greater" responder rate limitation impermissibly introduces new subject matter into each of the proposed substitute claims. As such, Patent Owner has not met the statutory and regulatory requirements for the revised MTA.

F. Unpatentability Grounds

With regard to the proposed substitute claims, Petitioner also raises multiple unpatentability grounds under 35 U.S.C. § 112 for lack of written description support, lack of enablement, and indefiniteness. Opp. 7–25. As it is dispositive to our conclusion, we focus our analysis on the written description and enablement grounds with respect to the "50% or greater" responder rate limitation.

1. Lack of Written Description

For the reasons we have discussed above with regard to the statutory and regulatory prohibition against new matter, we also find the proposed substitute claims are unpatentable under 35 U.S.C. § 112(a) for lack of written description support. *See Ariad*, 598 F.3d at 1348 (noting that the

prohibition against "adding new matter to the claims has properly been held enforceable under § 112, first paragraph").

2. Lack of Enablement

Petitioner separately argues that the proposed substitute claims are not enabled with respect to the "50% or greater" limitation. In assessing whether the claims satisfy the enablement requirement of 35 U.S.C. § 112(a), we consider the so-called "*Wands* factors": (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1998).

With respect to the quantity of experimentation necessary, Petitioner contends that:

> Given Dr. Singh's admission that substantial changes in excipients and neurotoxin can make it impossible to speculate whether a certain formulation would meet the claimed 50% threshold responder rate, a clinical study would need to be conducted for any formulation in which an excipient or the neurotoxin was changed, amounting to a research plan of trial and error.

Opp. 17 (citing Ex. 1106 ¶ 86); *see also id*. at 14 (citing Ex. 1089, 30:2–31:1, where Dr. Singh acknowledged that if you changed some of the formulation components, including the type of botulinum toxin A, it would be "impossible to speculate" whether the formulation would exhibit or meet the 50% responder rate limitation). As further evidence of the high amount of experimentation necessary, Petitioner points out that the substitute claims encompass formulations that contain abotulinumtoxinA, which requires a dose of 2.5 times the dose of 20U of BOTOX®, and thus "substantial

development work would be necessary to achieve the threshold responder rate with such a low dose of abobotulinumtoxinA." *Id.* at 17 (citing Ex. 1106 ¶ 87).

With respect to the amount of direction provided in the specification, Petitioner contends that "[t]he specification describes clinical data for MT10109 (in liquid and lyophilized forms) but does not teach a POSA how to modify MT10109 by changing the neurotoxin, the polysorbate, or the other stabilizer while still maintaining the threshold 16-week responder rate." *Id.* at 18 (citing Ex. 1106 ¶ 89).

With respect to the presence or absence of working examples, Petitioner contends that the specification provides only two working examples that exhibit very specific responder rates (52% and 62%) "tied to the specific formulations in a specific patient population." *Id.* (citing Ex. 1106 ¶ 90).

With respect to the nature of the invention and the state of the prior art, Petitioner contends that "[a]t the time of the '728 patent, there was nothing that would permit a POSA to correlate the formulation of any botulinum toxin composition with a 16-week responder rate of 50% or greater" and thus "the 16-week responder rate could only be determined by conducting a costly and expensive clinical trial." *Id.* at 18–19 (citing Ex. 1106 ¶¶ 91–92).

With respect to the relative skill of those in the art and predictability in the art, Petitioner contends that the parties agree that the level of skill in the art is relatively high, but contends that achieving the claimed 16-week responder rates is unpredictable. *Id.* at 19 (citing Ex. 1106 ¶¶ 93–94).

Finally, with respect to the breadth of the claims, Petitioner contends that the proposed substitute claims are "so broad that they include a large

number of potential botulinum toxin A compositions, but the specification provides no guidance as to which ones would exhibit the claimed 'greater duration of effect' (as measured by responder rates at 16 weeks using physician's live assessment) and which ones would not." *Id.* (citing Ex. 1106 ¶¶ 97–101). Petitioner points to Dr. Ramzan's testimony explaining that the "the teachings of the '728 patent do not establish any structure-function correlation between the ingredients (or their amounts) of a botulinum toxin A composition and its 16-week responder rate." *Id.* at 19–20. Petitioner also contends the '728 patent does not teach a person of ordinary skill in the art how to formulate any abobotulinum A neurotoxin composition that exhibits the claimed responder rate when administered in the same amount as 20U of BOTOX®." *Id.* at 21.

Patent Owner responds that the revised proposed substitute claims are enabled because Petitioner relies upon "the flawed proposition that clinical studies categorically require undue experimentation, while mischaracterizing the abilities of a POSA." Reply 9. According to Patent Owner, "[i]t would take no more than routine experimentation to confirm that similarly formulated toxin compositions meet the claimed duration limitation." *Id.* at 10 (citing Ex. 2062 ¶¶ 28–32). Patent Owner relies upon the testimony of its expert Dr. Middaugh as explaining "that in view of the disclosure of the '728 Patent, a POSA would expect other similar formulations containing polysorbate and a stabilizer to have a similarly greater length of effect compared to BOTOX®." *Id.* Patent Owner also contends that Petitioner's arguments are flawed insofar as the Federal Circuit does not require working examples to satisfy the enablement requirement and that such arguments rest on the mistaken premise that the claims require comparability between the claimed composition and 20U of BOTOX®. *Id.* at 11. Additionally, with

regard to proposed substitute claim 20 in particular, Patent Owner contends that a POSA would be able to replicate MT10109L without knowledge of Patent Owner's proprietary manufacturing process." *Id.* at 11–12.

Having considered the arguments and evidence of record, we determine that a preponderance of the evidence supports the conclusion that the full scope of the claims is not enabled. In particular, Petitioner has persuasively shown through the testimony of its expert Dr. Ramzan that, based on the guidance provided in the specification, a POSA would not have been able to achieve responder rates significantly higher than the exemplified 62% responder rate, including as high 85%, 95%, or even 100%, using the claimed animal-protein-free botulinum toxin formulations without undue experimentation. Ex. 1106 ¶¶ 85–101.

We find the *Magsil* case to be instructive. There, the court held that the claims were not enabled with respect to a limitation reciting "a change in the resistance by at least 10% at room temperature" when the specification only taught that the inventors were able to achieve a maximum change in resistance of 11.8%. *Magsil*, 687 F.3d at 1379–85. The court found that the specification only enabled an ordinarily skilled artisan to achieve a small subset of the claimed range, and the "[t]he open claim language chosen by the inventors does not grant them any forgiveness on the scope of required enablement." *Id.* at 1383–84.

Likewise, in *In re Fisher*, the court held that claims reciting an open-end range of a potency of "at least 1 International Unit of ACTH per milligram" were not enabled by a specification disclosing products having potencies from 1.11 to 2.30 International Units. 427 F.2d 833, 839 (CCPA 1970). The court in *Fisher* noted that:

> The issue thus presented is whether an inventor[] who is the first to achieve a potency of greater than 1.0 for certain types of compositions, which potency was long desired because of its beneficial effect on humans, should be allowed to dominate all such compositions having potencies greater than 1.0, including future compositions having potencies far in excess of those obtainable from his teachings plus ordinary skill.

Id. The court concluded "that appellant has not enabled the preparation of ACTHs having potencies much greater than 2.3, and the claim recitations of potency of 'at least 1' render the claims insufficiently supported under the first paragraph of 35 U.S.C. § 112." *Id.* Here, unlike the open-ended ranges at issue in *Magsil* and *Fisher*, we have interpreted the responder rate limitation to have an upper limit of 100%. But even with that bounded interpretation, we find nothing in the specification to suggest that a POSA would, absent undue experimentation, have been able to achieve responder rates much higher than the maximum responder rate of 62% disclosed in the examples of the '728 patent.

Although Patent Owner has argued that the claims are enabled with regard to other limitations, Patent Owner does not address the enablement arguments made with regard to the full scope of the responder rate limitation when it is interpreted to be a range of 50–100%. Rather, Patent Owner's arguments are based on the assumption that the responder rate limitation only requires a threshold of 50%, which we have rejected for the reasons stated above.

Accordingly, we conclude that the proposed substitute claims are unpatentable for lack of enablement under 35 U.S.C. § 112(a).

III. CONCLUSION

For the foregoing reasons, we conclude that Patent Owner has not met its burden of meeting the statutory and regulatory requirement against

introducing new matter in the proposed substitute claims. Additionally, we determine that Petitioner has demonstrated by a preponderance of the evidence that the proposed substitute claims are unpatentable under 35 U.S.C. § 112(a) for lack of written description support and lack of enablement.[3] Accordingly, we deny Patent Owner's revised Motion to Amend with regard to proposed substitute claims 19–27.[4] Original claims 1–10 of the '728 patent are cancelled by virtue of Patent Owner's non-contingent revised MTA.

In summary:

Motion to Amend Outcome	**Claim(s)**
Original Claims Cancelled by Amendment	1–10
Substitute Claims Proposed in the Amendment	19–27
Substitute Claims: Motion to Amend Granted	
Substitute Claims: Motion to Amend Denied	19–27
Substitute Claims: Not Reached	

IV. ORDER

In consideration of the foregoing, it is hereby:

[3] In view of our conclusion with regard to the "50% or greater" limitation, we do not reach the other unpatentability arguments with regard to the proposed substitute claims, including the *sua sponte* ground of unpatentability that we asked the parties to address at oral argument.

[4] Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding. *See* 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. *See* 37 C.F.R. § 42.8(a)(3), (b)(2).

ORDERED that original claims 1–10 of the ’728 patent are cancelled by virtue of Patent Owner’s non-contingent revised Motion to Amend;

FURTHER ORDERED that Patent Owner’s non-contingent revised Motion to Amend is denied as to proposed substitute claims 19–27; and

FURTHER ORDERED that, because this is a final written decision, parties to this proceeding seeking judicial review of our Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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