IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

United States Patent No.: 6,806,251	§	Attorney Docket No.:
Inventor: Gregory Blair Lamb	§	111682-0002-651
Formerly Application No.: 10/062,954	§	Customer No. 28120
Issue Date: Oct. 19, 2004	§	
Filing Date: Jan. 31, 2002	§	Petitioners: Allergan, Inc.;
Former Group Art Unit: 1648	§	Allergan Sales, LLC
Former Examiners: J. Housel; Z. Lucas	§	
	§	

For: METHOD OF TREATING PAIN

MAIL STOP PATENT BOARD
Patent Trial and Appeal Board
United States Patent and Trademark Office
Post Office Box 1450
Alexandria, Virginia 22313-1450

PETITION FOR *INTER PARTES* REVIEW OF UNITED STATES PATENT NO. 6,806,251

TABLE OF CONTENTS

LIST OF EXHIBITS

Exhibit	Description
Ex.1001	U.S. Patent No. 6,806,251
Ex.1002	File History of U.S. Patent No. 6,806,251
Ex. 1003	Declaration of Christopher Butler
Ex. 1003A	Exhibit A to the Declaration of Christopher Butler – Lamb, "DrLamb.com" (Oct. 18, 2000 archive of http://www.drlamb.com/)
Ex. 1003B	Exhibit B to the Declaration of Christopher Butler – Lamb, "Pain Topics" (Oct. 14, 2000 archive of http://drlamb.com/PainTopics.htm)
Ex. 1003C	Exhibit C to the Declaration of Christopher Butler – Lamb, "The Magic of Botox" (Oct. 28, 2000 archive of http://www.drlamb.com/magicbotox.htm)
Ex.1003D	Exhibit D to the Declaration of Christopher Butler – Lamb, "Botox and IMS for Intractable Headache" (Jan. 19, 2001 archive of http://drlamb.com/botoxheadaches.htm) ("B&H")
Ex.1003E	Exhibit E to the Declaration of Christopher Butler – Lamb, "Is There a Cure for Fibromyalgia?" (Oct. 19, 2000 archive of http://www.drlamb.com/curefibromyalgia.htm) ("Fibromyalgia")
Ex. 1003F	Exhibit F to the Declaration of Christopher Butler – Lamb, "Acupuncture For Pain Relief Puncture Accurately" (Oct. 12, 2000 archive of http://drlamb.com/Accupuncture.htm)
Ex. 1003G	Exhibit G to the Declaration of Christopher Butler – Lamb, "Ask Dr. Lamb" (Oct. 16, 2000 archive of http://drlamb.com/secondopinion.htm)
Ex. 1003H	Exhibit H to the Declaration of Christopher Butler – Lamb, "DrLamb.com" (Feb. 26, 2001 archive of http://www.drlamb.com/)
Ex. 1003I	Exhibit I to the Declaration of Christopher Butler – Lamb, "Pain Topics" (Feb. 5, 2001 archive of http://drlamb.com/PainTopics.htm)
Ex. 1003J	Exhibit J to the Declaration of Christopher Butler – Lamb, "The Magic of Botox" (Feb. 16, 2001 archive of http://www.drlamb.com/magicbotox.htm)
Ex. 1003K	Exhibit K to the Declaration of Christopher Butler – Lamb, "Botox and IMS for Intractable Headache" (Feb. 22, 2001 archive of http://drlamb.com/botoxheadaches.htm)
Ex. 1003L	Exhibit L to the Declaration of Christopher Butler – Lamb, "Is There a Cure for Fibromyalgia?" (Feb. 14, 2001 archive of http://www.drlamb.com/curefibromyalgia.htm)

Ex. 1003M	Exhibit M to the Declaration of Christopher Butler – Lamb, "Acupuncture For Pain Relief Puncture Accurately" (Feb. 17, 2001 archive of http://drlamb.com/Accupuncture.htm)
Ex. 1003N	Exhibit N to the Declaration of Christopher Butler – Lamb, "Ask Dr. Lamb" (Feb. 19, 2001 archive of http://drlamb.com/secondopinion.htm)
Ex. 1004	Cheshire *et al.*, "Botulinum toxin in the treatment of myofascial pain syndrome," PAIN 59, 65-69 (1994) ("Cheshire")
Ex. 1005	Declaration of Jacqueline Lewis
Ex. 1005A	Exhibit A to the Declaration of Jacqueline Lewis – Simons *et al.*, *Travell & Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual Volume 1. Upper Half of Body* (2d ed. 1999) ("Travell")
Ex. 1006	Certification of Sally Jennings
Ex. 1006A	Exhibit A to the Certification of Sally Jennings – excerpts from the Travell textbook
Ex. 1007	Declaration of Hayan Yoon
Ex. 1007A	Exhibit A to the Declaration of Hayan Yoon – Gunn, *The Gunn Approach to the Treatment of Chronic Pain: Intramuscular Stimulation for Myofascial Pain of Radiculopathic Origin* (2d ed. 1996) ("Gunn")
Ex. 1008	Declaration of Deborah Rae
Ex. 1008A	Exhibit A to the Declaration of Deborah Rae – excerpts from the Gunn textbook
Ex. 1008B	Exhibit B to the Declaration of Deborah Rae – the electronic record of a copy of the Gunn textbook cataloged in the University of Delaware Library
Ex. 1009	Physicians' Desk Reference (55th ed. 2001), Medical Economics
Ex. 1010	Mosby's Medical, Nursing & Allied Health Dictionary (5th ed. 1998), A Time Mirror Company
Ex. 1011	International Publication No. WO 94/15629 filed by Borodic ("Borodic")
Ex. 1012	Guyer, "Mechanism of Botulinum Toxin in the Relief of Chronic Pain," CURRENT REVIEW OF PAIN, 3:427-431 (1999) ("Guyer")
Ex. 1013	Bogduk, "Cervicogenic Headache: Anatomic Basis and Pathophysiologic Mechanisms," CURRENT REVIEW OF PAIN, 5:382-386 (2001) ("Bodguk")
Ex. 1014	Jansen, "Surgical treatment of non-responsive cervicogenic headache," CLIN. EXP. RHEUMATOL, 18:S67-S70 (2000) ("Jansen")

Ex. 1015	Sheldon, "Headache Patterns and Cervical Nerve Root Compression – A 15-Year Study of Hospitalization For Headache," HEADACHE 6(4):180-188 (1967) ("Sheldon")
Ex. 1016	Allergan's Answer (D.I. 30, dated July 30, 2015), *1474791 Ontario, Ltd. v. Allergan, Inc., et al.*, Case No. 1:15-cv-03372 (N.D. Ill.)
Ex. 1017	Declaration of Edgar Ross
Ex. 1018	Declaration of Richard Moncrief
Ex. 1019	Certification of Sally Jennings

I. INTRODUCTION

Pursuant to §§ 311-319 and § 42,[1] the undersigned, on behalf of and acting in a representative capacity for Allergan, Inc. and Allergan Sales, LLC (collectively "Allergan" or "Petitioners"), hereby petition for *inter partes* review of Claims 1-7 ("Challenged Claims") of U.S. Pat. No. 6,806,251 ("the '251"), currently assigned to 1474791 Ontario Limited ("Ontario").

The '251, which lists Gregory Blair Lamb ("Dr. Lamb") as the sole named inventor, is generally related to a method of injecting botulinum toxin (*e.g.*, Botox®[2]) into intrinsic spinal muscles for the treatment of pain. *See* Ex. 1001 at 2:3-10. As set forth in this Petition, the purported "invention" of the Challenged Claims was disclosed and taught in printed publications prior to the claimed priority date of January 31, 2002.

Dr. Lamb, himself, published two articles on his own website ("www.drlamb.com")[3] more than one year before the claimed priority date. The

---

[1] Section cites are to 35 U.S.C. or 37 C.F.R. as the context indicates, and all emphasis and annotations are added, unless otherwise noted.

[2] Botox® is a registered trademark of Allergan, Inc.

[3] Webpages published on "www.drlamb.com," captured and archived by the Wayback Machine between Oct. 12, 2000 and Feb. 26, 2001, are submitted as Attachments A-N to Exhibit 1003. These webpages were linked to the homepage

first is titled "Botox and IMS for Intractable Headache" on the webpage "Botox & Headaches" ("B&H"); the second is titled "Is There a Cure for Fibromyalgia?" on the webpage "Fibromyalgia" ("Fibromyalgia"). These articles, which Dr. Lamb affirmatively connected on his website by a hyperlink between them, disclosed the subject matter claimed by the '251– a method of injecting botulinum toxin into intrinsic muscles for the treatment of disorders associated with spinal compression. B&H discloses a protocol to treat chronic headaches associated with "nerve root irritation and spinal compression." Ex. 1003D at 1-2. Specifically, B&H discloses that "Botox" injection into the multifidus, which Dr. Lamb expressly defined as an intrinsic muscle in the '251 specification (Ex. 1001 at 3:7-15), "can help to break the constant spasm in this area, which commonly triggers the whole headache scenario." Ex. 1003D at 2. Similarly, Fibromyalgia discloses treatment with, among other things, "Botox" for a variety of disorders associated with spinal compression caused by "spastic" or "short" muscles, including, *inter alia*, compression neuropathy and disc herniation. Ex. 1003E at 2, 3, 6. Despite the clear relevance of his articles disclosing every limitation of at least one of the Challenged Claims

---

("drlamb.com"), B&H (http://drlamb.com/botoxheadaches.htm) and Fibromyalgia (http://www.drlamb.com/curefibromyalgia.htm) through one to three hyperlinks. *See, e.g.*, http://web.archive.org/web/20000829091101/http://www.drlamb.com/.

more than a year before filing the patent application, Dr. Lamb never disclosed them to the Examiner reviewing his patent application; thus, the articles have never previously been considered by the Patent and Trademark Office ("PTO"). As shown below, B&H anticipates and/or renders obvious all of the Challenged Claims, as set forth in Grounds 1 and 2. Fibromyalgia in view of B&H renders obvious all of the Challenged Claims, as set forth in Ground 4.

Likewise, an authoritative textbook in the relevant medical field of pain disorders by Simons *et al.*, titled "Travell & Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual Volume 1. Upper Half of Body" (2nd edition) and published in 1999 ("Travell"), anticipates and/or renders obvious all of the Challenged Claims, as set forth in Grounds 6 and 7. Travell also discloses a method of treating disorders associated with spinal compression by injecting botulinum toxin into intrinsic muscles. *See* Ex. 1005A at Chapters 3, 16 and 48. Like B&H and Fibromyalgia, Travell has not previously been considered by the PTO. Furthermore, an article by Cheshire *et al.*, titled "Botulinum toxin in the treatment of myofascial pain syndrome," PAIN 59, 65-69 (1994) ("Cheshire"), which was specifically cited and reviewed in Travell, discloses a clinical study where botulinum toxin injection was successfully used in treating patients with pain disorders. Cheshire further discloses a specific protocol used in the study, including effective dosages and number of injections. *See, e.g.*, Ex. 1004 at 67-68; *see also* Ex. 1005A at 155,

174. Thus, the primary references—B&H, Fibromyalgia, and/or Travell—in view of the teachings of Cheshire render obvious Claims 5 and 6, as set forth in Grounds 3, 5, and 8.

During prosecution of the '251, in an attempt to avoid continued rejection of the claims, Applicant amended the claims to require administration of botulinum toxin "directly and solely" to the intrinsic muscles. *See* Ex. 1002 at 26-27 (5/25/2004 Response at 2-3). Examiner then allowed issuance of the claims, explaining that "this amendment to the claims is the ***sole*** ground for allowance." *See* Ex. 1002 at 8 (6/14/2004 Notice of Allowance at 3). But the prior art references cited herein, which have never been disclosed to the Examiner, make it clear that this "directly and solely" limitation was disclosed in, or at minimum clearly rendered obvious, by the art well before the earliest claimed priority date, and the Challenged Claims are neither novel nor non-obvious. *See, e.g.*, Ex. 1003D at 2; Ex. 1003E at 3, 6; Ex. 1005A at 150-151, 155, 164, 447, 466; *see also* Ex. 1017.

As demonstrated in this Petition, each and every element of the Challenged Claims, arranged as claimed, is found in a single prior art reference. In addition, each of these elements was at minimum well-known to any person of skill in the

art ("POSITA"),[4] and all of the Challenged Claims are, at best, no more than a routine and predictable combination of these well-known elements. Thus, Petitioners respectfully request that the Board find each of the Challenged Claims invalid under § 102 and/or § 103.

II. MANDATORY NOTICES UNDER § 42.8

Real Party in Interest Under § 42.8(b)(1). The real parties-in-interest are Allergan, Inc. and Allergan Sales, LLC (Petitioners), and Allergan plc.

Related Matters Under § 42.8(b)(2). Ontario has asserted claims of the '251 against Petitioners in *1474791 Ontario, Ltd. v. Allergan, Inc., et al.*, Case No. 1:15-cv-03372 (N.D. Ill., filed April 16, 2015) ("the Litigation").

Lead and Back-Up Counsel Under §§ 42.8(b)(3) and (4). Designated in the signature block.

III. PETITIONERS HAVE STANDING

A. Grounds for Standing Under § 42.104(a)

Petitioners certify pursuant to 37 C.F.R. § 42.104(a) that the '251 is eligible for (and that Petitioners are not barred or estopped from requesting) *inter partes* review. Petitioners were served with a Complaint asserting infringement of

[4] Throughout this petition, "the knowledge of the POSITA" refers to the knowledge that any POSITA possessed as of the time of the claimed invention, and relevant education and background for a POSITA is discussed *infra* Section V.B.

the ’251 on or after April 20, 2015, and neither Petitioners nor any other real party-in-interest, nor privy of Petitioners, was served with a Complaint before that date, or has initiated a civil action challenging validity of the ’251.

B. Claims and Statutory Grounds Under §§ 42.22 and 42.104(b)

Petitioners request *inter partes* review of Claims 1-7 and assert that these claims are unpatentable under §§ 102 and/or 103 as set forth below: ***Ground 1:*** Claims 1, 2, 4, 5, and 7 are anticipated by B&H; ***Ground 2:*** Claims 1-7 are obvious over B&H in view of the knowledge of a POSITA; ***Ground 3:*** Claim 6 is obvious over B&H in view of Cheshire; ***Ground 4:*** Claims 1-7 are obvious over Fibromyalgia in view of B&H; ***Ground 5:*** Claim 6 is obvious over Fibromyalgia in view of B&H and Cheshire; ***Ground 6:*** Claims 1-4, 6, and 7 are anticipated by Travell; ***Ground 7:*** Claims 1-4, 6, and 7 are obvious over Travell in view of the knowledge of a POSITA; ***Ground 8:*** Claim 5 is obvious over Travell in view of Cheshire.

Section V.C. provides claim charts specifying how the cited prior art anticipates or renders obvious each of the Challenged Claims, as confirmed by the knowledge and understanding of a POSITA at the time of the claimed invention as evidenced in Ex. 1017, the Declaration of Dr. Edgar L. Ross, M.D.

IV. SUMMARY OF THE '251 PATENT AND ITS FIELD

A. Overview of the '251 Patent

The '251 specification generally describes a "Method of Treating Pain," comprising the injection of botulinum toxin into the intrinsic spinal muscles. The '251's alleged invention is described as "a method of specifically treating [intrinsic] muscles thereby enabling the spine to relax and healing to occur." *See* Ex. 1001 at 3:22-24. The "intrinsic muscles," specifically defined in the '251 as the multifidus and the rotator brevis and longus muscles (*id.* at 3:1-15), are described as "deep spinal muscles surrounding the vertebrae and disks" (*id.* at 1:26-31). The specification further states, "The multifidus **18** and rotator **20** muscles, referred to herein as the intrinsic muscles, are very strong but also very small." *Id.* at 3:14-15. The muscles are shown in Figure 1 of the '251:

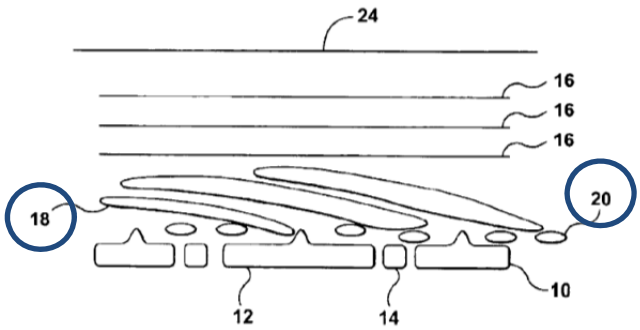


FIG. 1

According to the '251, very low doses of botulinum toxin, preferably Botox®, can be injected into these intrinsic muscles for the treatment of various "local or referred pain syndromes caused by chronic pain from the intrinsic muscles of the spine either directly or indirectly." *Id.* at 6:5-9. The mentioned pain syndromes include disc herniation and myofascial compression/traction neuropathies of the spine, the latter of which is associat-

ed with conditions like migraine headache and radiculopathy. *See id.* at 5:12-24. The '251 specification notes, "The injection causes the multifidus muscle **18** and rotator brevis and longus muscles **20** to relax, despite their propensity for reoccurring spasm," thus reducing neuropathy and radiculopathy "and their complications and side effects." *See id.* at 4:11-19.

The Challenged Claims are directed to a method of treating a disorder associated with spinal compression by administrating botulinum toxin "directly and solely to the intrinsic muscles." *Id.* at cl.1. Dependent claims 2-7 further narrow this method of treatment. For example, claims 2 and 3 list a group of disorders to be treated (*see id.* at cls. 2 ("compression neuropathies, … disc herniation, and degenerated discs") and 3 ("disc herniation or degenerated discs")), claim 4 provides a serotype ("botulinum toxin A") of botulinum toxin, claim 5 provides dosage amount ("between 1 and 30 mouse units") per injection site, and claims 6 and 7 provide the number of injection(s) required (*see id.* at cls. 6 ("a single injection") and 7 ("a plurality of injections")). *See generally* Ex. 1017 ¶¶25-26.

As detailed below, these features and the remaining aspects of the Challenged Claims were all already well-known in the art long before the earliest priority date listed on the face of the '251 (January 31, 2002). *See* Ex. 1017 ¶45. Indeed, the specification itself makes clear that the Applicant for the '251 did not purport to invent, *inter alia*, the following claim elements: <u>*Botulinum toxin A (e.g.,*</u>

Botox®) (*see, e.g.*, Ex. 1001 at 1:33-38); *use of botulinum toxin in the treatment of pain* (*see, e.g.*, *id.* at 1:53-57); *targeted administration of botulinum toxin* (*see, e.g.*, *id.* at 1:45-47); *involvement of intrinsic muscles in spinal compression* (*see, e.g.*, *id.* at 3:16-22).

B. Overview of the '251 Patent Prosecution History

The application that led to the '251, U.S. Patent App. No. 10/062,954 ("'954 Application") was filed on January 31, 2002, and lists Dr. Lamb as the sole inventor. The Examiner initially rejected all pending claims as obvious. Applicant responded by attempting to distinguish the pending claims from the cited art, arguing that "none of the cited references either alone or in combination suggests ***injecting the toxin directly into the intrinsic muscles***." Ex. 1002 at 109 (10/30/2003 Response at 6). Applicant also argued, "In the present invention, unlike the cited references, referred pain and dysfunction are reduced by indirect means of reducing vertebral and disk decompression." *Id.* The Examiner disagreed and affirmed the rejections of all pending claims as obvious. In addition to the previously cited prior art, the Examiner also relied on U.S. Patent No. 5,053,005 ("the '005 Patent"), noting that the '005 Patent "indicates that the ***multifidus muscle*** is included in reference to the paraspinal muscles, and indicates that ***those in the art were in possession of the knowledge necessary for injection of the toxin to the muscles***." Ex. 1002 at 46 (1/27/2004 Final Rejection at 6). Applicant then amended the inde-

pendent claims to require administration of botulinum toxin "directly and solely" to the intrinsic muscles, arguing this was not disclosed in the cited references. *See id.* at 30 (5/25/2004 Response at 6). The Examiner then allowed the claims, explaining that allowance was "limited to the fact that the claims have now been amended such that they require the administration botulinum toxin 'directly and solely' to the intrinsic muscles of a patient." *See id.* at 7 (6/14/2004 Notice of Allowance at 2). The '251 issued on October 19, 2004, based on the art then before the Examiner. Notably, this did ***not*** include the references cited herein, including publications from the Applicant, clearly showing the alleged invention was well-known more than a year prior to the filing of the '954 Application.

C. Overview of the Field of the Claimed Invention

It was well-known before January 31, 2002, that botulinum toxin could be used therapeutically to treat diverse disorders involving pain. *See, e.g.*, Ex. 1001 at 1:53-54 ("the use of botulinum toxin in the treatment of chronic pain is known"); Ex. 1012 at 427 ("There is an extremely voluminous literature on the clinical use of botulinum toxin."); *see also* Ex. 1017 ¶40. And practitioners had already used botulinum toxin to treat patients with pain disorders. *See, e.g.*, Ex. 1003D at 2; Ex. 1005A at 155; Ex. 1003E at 6; Ex. 1011 at 5; *see also* Ex. 1017 ¶40. A number of such successful clinical applications were widely reported in various clinical journals, websites and textbooks. *See, e.g.*, Ex. 1004; Ex. 1005A at 155; Ex. 1003D at

2; Ex. 1011. Those reports usually included explanation about specific treatment procedures that were found to be effective in treating patients. *See, e.g.*, Ex. 1004 at Summary, 67, 68 (disclosing the number of injections ("single, low-dose, trigger point injection"), dosages of injection ("50 mouse units … divided equally among 2 or 3 sites") and the serotype of botulinum toxin ("botulinum toxin type A")); *see also* Ex. 1011 at 8, 10 (disclosing the number of injections ("administered as a plurality of injections"), dosages of injection ("about 5 international units (IU) to about 1000 IU") and the serotype of botulinum toxin ("Pharmaceutical grade type A toxin"); *see also* Ex. 1017 ¶40.

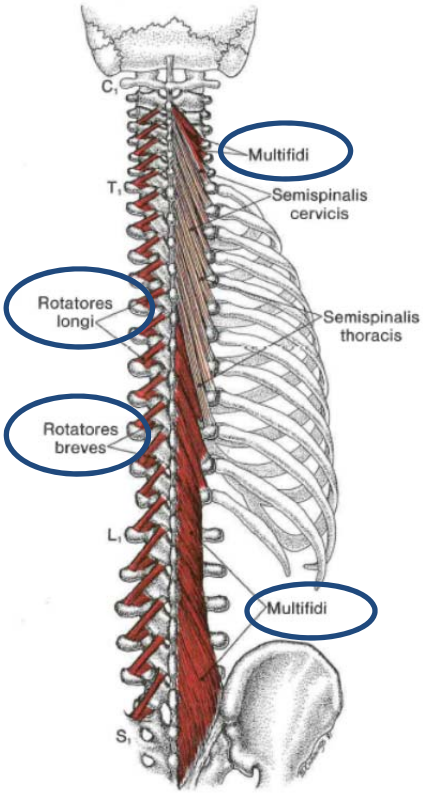
It was also well-known that botulinum toxin had paralytic effects even to normal muscles, as acknowledged by the '251 itself. *See, e.g.*, Ex. 1001 at 1:53-57 ("Although the use of botulinum toxin in the treatment of chronic pain is known, there can be serious side effects …. Unless the toxin is very specifically delivered to a particular muscle, there can be diffusion effects."); *see also* Ex. 1017 ¶41. Thus, it was well known to be important to administer botulinum toxin in a small volume specifically targeted to a muscle of therapeutic interest, minimizing diffusion to surrounding muscles or tissues. *See, e.g.*, Ex. 1005A at 155 ("It is important when using BTA [("botulinum toxin A")] to inject the minimum amount necessary and only in the TrP [("trigger point" in a muscle)], since BTA destroys normal and dysfunctional TrP endplates alike. Ottaviani and Childers emphasized

the importance of injecting BTA only where endplates were located"); Ex. 1003C at 2 ("It is also important for those who are injecting or are being injected with Botox to understand that there are risks. … That is to say, Botox will paralyze the muscle for up to three months or longer. There is no going back."); *see also* Ex. 1017 ¶41.

Furthermore, it was well known that a small volume of botulinum toxin administered via one or two injections can have therapeutic effect. *See, e.g.*, Ex. 1005A at 164 ("Recently activated (acute) myofascial TrPs that have no perpetuating factors or additional tissue damage because of mechanical injury to other tissues (i.e., TrPs that are uncomplicated) should resolve with one or two injections."); *id.* at 150-51 ("Some clinicians depend on the injection of large amounts of seriously myotoxic drugs like Botulinum toxin A … [but] it is much better to inject small amounts precisely where the contraction knots of the TrP are located."); Ex. 1004 at 68 ("Local blockade of neuromuscular transmission by single, low-dose, trigger point injection of botulinum toxin appears to be effective in the treatment of some patients with chronic myofascial pain disorders affecting cervical paraspinal and shoulder girdle musculature."); *see also* Ex. 1017 ¶42.

One group of muscles described as a target of such treatment using botulinum toxin was the deep paraspinal muscles, which include the multifidus and rotatores. *See, e.g.*, Ex. 1003D ("multifidus injections"); Ex. 1005A at 466 ("Location

3 of Figure 16.1A and D illustrates a common location and pain pattern of TrPs in the multifidus. When injecting this TrP …"); *id.* at Figure 16.9 ("Injection of the location in the left posterior cervical muscles near the C_4 level where one may encounter trigger points of the middle semispinalis capitis, semispinalis cervicis, multifidi, and rotatores muscles."); Ex. 1011 at 12 ("Multifidi Refers pain to back of neck"); *see also* Ex. 1017 ¶43. The multifidus is a deep paraspinal muscle "located approximately halfway between a spinous process and a lower traverse process." *See* Ex. 1005A at 455. The rotatores "arise from the transverse process of one vertebra and insert into the base of the spinous process of the vertebra above." Ex. 1007A at 82 (*see also* Exs. 1007; 1008; 1008A-B; 1019). *See also* Ex. 1005A at 919 (Fig. 48.4) (*see* left). The '251 refers to the multifidus and the rotatores as the "intrinsic muscles." Ex. 1001 at 3:7-15. *See also* Ex. 1017 ¶41.



It was well understood that botulinum toxin has analgesic effects by releasing the muscle spasms or shortening. *See, e.g.*, Ex. 1012 at 430 ("injection of botulinum toxin … possess[es] analgesic properties. The most obvious mechanisms … are through reduction of muscle spasm"); Ex. 1003D at 2 ("Deep multifidus in-

jections … can help to break the constant spasm"); *see also* Ex. 1007A at 6 ("The term 'spasm' is commonly used to describe muscle shortening …"); Ex. 1017 ¶44. The prior art taught that spasms or shortening of the intrinsic muscles (*i.e.*, deep paraspinal muscles, namely the multifidus and rotatores) were associated with pain disorders, in particular, those associated with spinal compression. *See, e.g.*, Ex. 1007A at 15 ("The deep muscles of the spine –semispinalis, multifidus, and rotatores– are probably the most important"); Ex. 1003E at 3 ("These deep muscles, primarily the multifidus and the rotator brevis and longus muscles are probably the most important muscles of the body."). For example, shortening of paraspinal muscles was well known to create a self-perpetuating circle – shortened muscles compress discs, which can cause narrowing of the intervertebral foramina, which irritates the nerve root, which causes neuropathy, which in turn leads to pain and further shortening of target muscles including paraspinal muscles. *See, e.g.*, Ex. 1007A at 7-8, 109. Increased pressure from shortened muscles was further known to eventually cause disorders such as facet-joint syndrome (*see id.* at 7) or disc degeneration and a prolapsed disc (*id.* at 29). *See also* Ex. 1007A at 115 ("Table 1: Shortened muscles in common syndromes" showing that "e.g. rotatores, multifidi, semispinalis" are associated with facet syndrome and intervertebral disc syndrome.). Furthermore, a ruptured intervertebral disc was known to cause nerve compression which would induce development of trigger points (*i.e.*, focal areas of

tenderness and pain in shortened muscles). *See* Ex. 1005A at 112; Ex. 1007A at 109. Thus, the prior art taught to a person of ordinary skill in the art that a treatment method for relieving muscle spasms or shortening could be applied for the treatment of pain disorders associated with spinal compression. *See* Ex. 1017 ¶44.

V. THERE IS A REASONABLE LIKELIHOOD THAT PETITIONERS WILL PREVAIL WITH RESPECT TO AT LEAST ONE CLAIM OF THE '251 PATENT

Petitioners submit there is at least "a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." § 314(a). Indeed, all of the Challenged Claims of the '251 are unpatentable because they are anticipated by and/or obvious in light of the prior art, as explained below in Sections V.C. to V.E. Specifically, this Petition relies on three primary references—B&H (Ex. 1003D), Fibromyalgia (Ex. 1003E), and Travell (Ex. 1005A)—that were never identified or discussed during prosecution. As detailed below, pursuant to 37 C.F.R. § 42.104(b)(4)-(5), all of the Challenged Claims are unpatentable.

A. Claim Construction Under § 42.104(b)(3)

Pursuant to § 42.100(b), and solely for purposes of this review, Petitioners construe the claim language such that terms are given their broadest reasonable interpretation ("BRI") in light of the specification. Terms not specifically listed and construed below should be given their plain and ordinary meaning under the BRI.

See 37 C.F.R. § 42.100(b). Because the standard for claim construction at the PTO is different than that used in U.S. District Court litigation, *see In re Am. Acad. of Sci. Tech Ctr.*, 367 F.3d 1359, 1364, 1369 (Fed. Cir. 2004); MPEP § 2111, Petitioners expressly reserve the right to argue in a different forum a different claim construction for any term in the '251 as appropriate in that proceeding.

As used in the Challenged Claims, for purposes of this review:

- ***"directly and solely"*** (Claim 1) should be construed to mean "straight into a muscle in a manner that minimizes diffusion of the toxin to surrounding muscles or tissue." This is supported by the '251, which explains that, because botulinum toxin is a paralytic neurotoxin with known potential side effects, it should be specifically delivered to a particular muscle in a manner that avoids the risk of diffusion to other tissue. *See, e.g.*, Ex. 1001 at 1:53-67; 4:46-55; Ex. 1017 ¶¶35-36. [5]

[5] In the Litigation, Allergan has asserted that "solely" is indefinite to the extent it is argued (as Patent Owner has) that the term is directed to excluding injection of one muscle group followed by injection of another muscle group. This improperly narrow construction is incorrect and not supported by the claim language or specification of the '251, and, although the claims are rendered obvious by the art cited herein under either reading, Petitioners submit the proper construction for review

- ***"intrinsic muscles"*** (Claim 1) should be construed to mean "the multifidus and rotator brevis and longus muscles," based on the express definition provided by Applicant as his own lexicographer *See, e.g.*, Ex. 1001 at 1:26-29, 3:7-15, 7:7-9, 7:24-26; Ex. 1017 ¶¶37-38.

B. Level of Ordinary Skill in the Art

The applicable person of ordinary skill in the art would have had a medical degree with at least three years of experience in treating patients, particularly patients with pain disorders. *See* Ex. 1017 ¶¶28-32.

---

purposes is as specified above. Allergan has also asserted that "effective dose" is indefinite because the '251 does not inform a POSITA of the outer boundaries of what is "effective." No construction is required here, however, because, regardless of the vagueness of the outer bounds of "effectiveness," the prior art relied on herein clearly discloses that the treatments described therein used "an effective dose." Finally, Allergan has asserted in the Litigation that "a patient in need of such therapy" is indefinite because the boundaries of what would render a patient "in need of" therapy are not reasonably clear. Again, no construction is required for purposes of this review because the prior art relied on herein clearly discloses that the treatments are used on patients expressly in need of therapy.

C. Grounds for Unpatentability

1. <u>Ground 1:</u> Claims 1, 2, 4, 5, and 7 are anticipated by B&H; <u>Ground 2:</u> Claims 1-7 are obvious over B&H in view of the knowledge of a POSITA

a. Overview of Botox & Headaches

Although never disclosed to the Examiner during prosecution, Applicant Dr. Lamb published B&H ***on his own website*** ("www.drlamb.com") where it was publicly available as of at least January 19, 2001, making it prior art to the '251 under at least § 102 (b). *See* Ex. 1003; 1003D; *see also* Ex. 1017 ¶46. B&H expressly disclosed the subject matter of Claims 1, 2, 4, 5, and 7 more than one year before the January 31, 2002 filing date of the '251. B&H describes, among other things (Ex. 1003D at 1-2; *see also* Ex. 1017 ¶47):

- The treatment of "chronic headache" associated with "nerve root irritation" and "spinal compression";
- "[U]s[ing] Botox in the deep cervical spine in hopes to release severe and chronic cervical disease in the neck";
- "Deep multifidus injections";
- "[V]ery low doses" of "Botox" (*i.e.*, "1.25 units or even lower") that "can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."

Despite its clear relevance, B&H was never disclosed to the Examiner. Quite to the contrary, by late 2001 or early 2002, prior to filing the '954 Application, Dr. Lamb had removed the link to B&H from www.drlamb.com.[6]

b. Claim Charts for Ground 1 (Claims 1, 2, 4, 5, and 7 are anticipated by B&H) and Ground 2 (Claims 1-7 are obvious over B&H in view of the knowledge of a POSITA)

cl. 1	**Prior Art**
1. A method of treating a disorder associated with spinal compression comprising[7]	**B&H discloses a method of treating a disorder associated with spinal compression (*e.g.*, "nerve root irritation," "chronic headache," and "severe and chronic cervical disease in the neck").** *See, e.g.*, Ex. 1003D at 1 ("The result is a predictable increase in deep neck tension, which probably causes an increase in ***nerve root irritation*** and ***spinal compression***. Pain and dysfunction will likely refer to the head in the form of skull muscle spasm, intracranial vessel spasm and direct referred pain from the neck."); *id.* ("Botox predictably can be used both in the head and neck to help block and probably ***treat*** long term ***chronic headache***."); *id* at 2 ("About two years ago, we first used Botox in the deep cervical

[6] Although not cognizable as a ground in this *inter partes* review, these actions form the basis of Petitioner's allegations of inequitable conduct in *1474791 Ontario, Ltd. v. Allergan, Inc., et al.*, Case No. 1:15-cv-03372 (N.D. Ill., filed April 16, 2015). *See* Ex. 1016.

[7] For all grounds, to the extent Claim 1's preamble is deemed a limitation, the evidence identified herein shows it was disclosed or at minimum would have been obvious to a POSITA.

	spine in hopes to release ***severe and chronic cervical disease*** in the neck. Since then, the Botox protocol we are currently using for the ***treatment of chronic intractable headache*** at the Lamb Pain Clinic is as follows-"); *id.* (Deep multifidus injections at C2 to C3 area with very low doses of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the ***whole headache scenario***."). *See also* Ex. 1017 ¶¶48-52.
[1-1] administering an effective dose of botulinum toxin	**B&H discloses administering an effective dose (*e.g.*, "1.25 units," "successful route to get back a maximum quality of life," and "help to break the constant spasm in this area, which commonly triggers the whole headache scenario") of botulinum toxin (*e.g.*, "botulinum toxin or Botox").** *See, e.g.*, Ex. 1003D at 2 ("About two years ago, we first used ***Botox*** in the deep cervical spine in hopes to release severe and chronic cervical disease in the neck. Since then, the Botox protocol we are currently using for the treatment of chronic intractable headache at the Lamb Pain Clinic is as follows- First dilute 100 units of the ***botulinum toxin or Botox*** into 4cc of non-preserved normal saline. This allows for 2.5 units in each 0.1 c.c.'s of fluid."); *id.* ("***[I]njection therapy*** with IMS and ***Botox*** can be a ***successful route to get back a maximum quality of life***."); *id.* ("Deep multifidus injections at C2 to C3 area with very low ***doses of 1.25 units*** or even lower can ***help to break the constant spasm in this area, which commonly triggers the whole headache scenario***."). *See also* Ex. 1017 ¶¶53-54.
[1-2] directly and solely to the intrinsic muscles of a patient in need of such therapy.	**B&H discloses administering botulinum toxin directly and solely to the intrinsic muscles (*e.g.*, "[d]eep multifidus injections at C2 to C3 area") of a patient in need of such therapy (*e.g.*, "injection therapy . . . to get back a maximum quality of life").** *See, e.g.*, Ex. 1003D at 2 ("First dilute 100 units of the ***botulinum toxin or Botox*** into 4cc of non-preserved normal saline. … Deep ***multifidus injections*** at C2 to C3 area with very low doses of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."); *id.* ("***[I]njection therapy*** with IMS and Botox can be a successful route ***to get back a maximum quality of life***."). *See also* Ex. 1017 ¶¶55-58.

B&H discloses all of the limitations of Claim 1. *See* Ex. 1017 ¶¶48-58. Regarding the preamble, B&H discloses treatment of "chronic headache," "nerve root irritation," and "spinal compression," which are all "disorder[s] associated with spinal compression." *See* Ex. 1003D at 1-2; Ex. 1017 ¶¶48-50. For example, a POSITA would have understood from B&H that "pain and dysfunction" from spinal compression "refer[s] to the head" (*i.e.*, referred pain is felt in a location (the head) other than its source (compression in the spine)) in the form of headache; thus, the headache of B&H is a disorder associated with spinal compression. *See* Ex. 1003D at 1; *see also* Ex. 1013 at 382; Ex. 1014 at S67; Ex. 1015 at 1; Ex. 1017 ¶49. A POSITA would also have understood that "nerve root irritation and spinal compression" is a type of "compression neuropathy" disorder associated with spinal compression. *See* Ex. 1010 at 377; *see also* Ex. 1017 ¶50.

To the extent it is argued that any further disclosure is required to meet the preamble, the preamble would at minimum have been obvious to a POSITA from the disclosures of B&H in light of the knowledge of a POSITA for at least two reasons. First, at minimum, in light of B&H's teachings, it would have been obvious to a POSITA to use botulinum toxin to treat a disorder associated with spinal compression, especially because, among other things, disorders associated with spinal compression in general are characterized by similar pathophysiology as the chronic headache and nerve root irritation disorders named in B&H and thus would have

been reasonably expected to respond to similar treatment. Ex. 1017 ¶51. Second, in addition to the disclosures discussed above, B&H states "Botox" was used "in the deep cervical spine" to treat "severe and chronic cervical disease in the neck," which a POSITA would have understood to be referring to a "disorder associated with spinal compression," such as disc herniation, degenerative discs, facet joint arthritis or facet joint degeneration, or, at minimum, a POSITA would have understood from this teaching that "Botox" could have been used to successfully treat such disorders. *See* Ex. 1003D at 1-2; Ex. 1017 ¶52.

Regarding Element [1-1], B&H discloses administering an effective dose of botulinum toxin. *See* Ex. 1017 ¶53. For example, B&H describes a "Botox protocol we are currently using for the treatment of chronic intractable headache at the Lamb Pain Clinic" and discloses that "[d]eep multifidus injections . . . with very low doses of 1.25 units . . . can help to break the constant spasm in this area, which commonly triggers the whole headache scenario." Ex. 1003D at 2. B&H also discloses that "injection therapy with IMS and Botox can be a successful route to get back a maximum quality of life." *Id.* Thus, this limitation is expressly disclosed. *See* Ex. 1017 ¶53. At minimum, in light of these disclosures, this limitation would have been obvious to a POSITA, who would have been motivated and found it obvious to use a dose that would be effective to treat the disorder, such as "chronic

headache" and "severe and chronic cervical disease in the neck" identified in B&H, in implementing the method disclosed in B&H. Ex. 1017 ¶54.

Regarding Element [1-2], B&H discloses to a POSITA that botulinum toxin can be administered "directly and solely" to the intrinsic muscles (*e.g.*, the multifidus) of a patient in need of therapy. *See* Ex. 1017 ¶¶55-56. For example, B&H discloses that "[d]eep multifidus injections . . . with very low doses of 1.25 units . . . can help to break the constant spasm in this area, which commonly triggers the whole headache scenario." Ex. 1003D at 2. Thus, B&H discloses administering "Botox" straight into the multifidus of a patient with chronic headache with a low dose of 1.25 units in a small volume of 0.05 c.c.'s, which a POSITA would have understood would minimize diffusion of the toxin into surrounding muscle or tissue. *See* Ex. 1017 ¶¶55-56.

To the extent it is argued any further disclosure is required to meet Element [1-2], Element [1-2] would at minimum have been obvious to a POSITA from the disclosures of B&H in light of the knowledge of a POSITA. *See* Ex. 1017 ¶57. First, under Petitioners' proposed construction, in light of the teachings of B&H, it would have been obvious to a POSITA to administer botulinum toxin straight into the multifidus in a manner that would minimize diffusion of the toxin into surrounding tissue, regardless of whether the method is applied for treating "chronic headache" or "severe and chronic cervical disease in the neck." *Id.* This is espe-

cially true because, as acknowledged in the '251 itself, it was known in the art that botulinum toxin is a powerful paralytic neurotoxin that may cause serious side effects, and a POSITA would have understood that diffusion is to be avoided or minimized. *See, e.g.*, Ex. 1001 at 1:53-60; Ex. 1004 at 66; Ex. 1005A at 155, 150-151; Ex. 1003C; Ex. 1003D at 2; *see also* Ex. 1017 ¶57. Second, even if the term "directly and solely" is construed narrowly to require administration only to the intrinsic muscles (and not to other muscle groups) during a given treatment session, it still would, at minimum, have been obvious to a POSITA, in view of the teachings in B&H, to use botulinum toxin only in the multifidus muscle where that muscle was the source of "spasm" contributing to a disorder associated with spinal compression. *See* Ex. 1003D at 2 (disclosing the constant spasm in the multifidus muscles "commonly triggers the whole headache scenario"); *see also* Ex. 1017 ¶58. Such treatment would have had a reasonable expectation of success because botulinum toxins were well-known to have analgesic properties through reduction of muscle spasm. *See* Ex. 1012 at 430; Ex. 1005A at 151; *see also* Ex. 1017 ¶58.

cl. 2	**Prior Art**
2. A method according to claim 1, wherein said disorder associated with spinal compression is selected from the group consisting of com-	*See, e.g.*, claim 1. **B&H discloses a method of treating a disorder associated with spinal compression selected from the group consisting of compression neuropathies, facet joint disease of the spin [*sic*], sciatica, disc herniation, and degenerated discs (*e.g.*, "nerve root irritation" and "severe and chronic cervical disease in the neck").** *See,*

pression neuropathies, facet joint disease of the spin [*sic*], sciatica, disc herniation, and degenerated discs.	*e.g.*, Ex. 1003D at 1 ("The result is a predictable increase in deep neck tension, which probably causes an increase in ***nerve root irritation*** and ***spinal compression***."); *id*. at 2 ("About two years ago, we first used Botox in the deep cervical spine in hopes to release ***severe and chronic cervical disease*** in the neck."). *See also* Ex. 1017 ¶¶59-63.

B&H discloses Claim 2's added limitation. *See* Ex. 1017 ¶¶60-63. As noted above, a POSITA would have understood that "nerve root irritation and spinal compression" is a type of compression neuropathy, which is a disorder associated with spinal compression. *See* Ex. 1010 at 377; Ex. 1017 ¶61. To the extent it is argued any further disclosure is required, Claim 2's added limitation would at minimum have been obvious to a POSITA from these express disclosures in light of the knowledge of a POSITA, for at least the reasons set forth in the discussion of the preamble of Claim 1. *See* Ex. 1017 ¶¶62-63

cl. 3	**Prior Art**
3. A method according to claim 2, wherein the disorder is disc herniation or degenerated discs.	*See, e.g.*, claims 1 and 2. **B&H discloses a method of treating a disorder such as disc herniation or degenerated discs (*e.g.*, "severe and chronic cervical disease in the neck").** *See, e.g.*, Ex. 1003D at 2 ("About two years ago, we first used Botox in the deep cervical spine in hopes to release ***severe and chronic cervical disease*** in the neck."). *See also* Ex. 1017 ¶¶64-65.

B&H in light of the knowledge of a POSITA renders obvious Claim 3's added limitation, for at least the reasons set forth in the discussion of the preamble of Claim 1 and Claim 2. *See* Ex. 1017 ¶¶64-65. First, in light of B&H's teachings,

it would have been obvious to a POSITA to use botulinum toxin to treat disc herniation or degenerated discs, especially because, among other things, disc herniation or degenerated discs were known to have similar pathophysiology as the chronic headache and nerve root irritation disorders named in B&H and thus would have been reasonably expected to respond to similar treatment. *See* Ex. 1017 ¶¶65, 63. Second, in addition to the disclosures discussed above, B&H states "Botox" was used "in the deep cervical spine" to treat "severe and chronic cervical disease in the neck," which a POSITA would have understood to be referring to a "disorder associated with spinal compression," such as disc herniation and/or degenerative discs. *See* Ex. 1003D at 1-2; Ex. 1017 ¶¶65, 62.

cl. 4	**Prior Art**
4. A method according to claim 1, wherein said botulinum toxin paralyzing agent is botulinum toxin A.	*See, e.g.*, claim 1. **B&H discloses a method of administering botulinum toxin A (*e.g.*, "Botox").** *See, e.g.*, Ex. 1003D at 2 ("First dilute 100 units of the ***botulinum toxin or Botox*** into 4cc of non-preserved normal saline."). *See also* Ex. 1017 ¶¶66-69.

B&H discloses Claim 4's added limitation. *See* Ex. 1017 ¶¶66-69. A POSITA would have understood B&H's disclosure of "Botox" to refer to "botulinum toxin A" because Botox® has been a trade name for a form of botulinum toxin type A commercialized by Allergan since well before January 2002. *See, e.g.*, Ex. 1009 at 515; Ex. 1003D at 2; Ex. 1003C; *see also* Ex. 1017 ¶68. To the extent

it is argued any further disclosure is required, this would at minimum have been obvious to a POSITA from these express disclosures in light of the knowledge of a POSITA, who would have found it obvious to use botulinum toxin A in implementing the method disclosed in B&H, because botulinum toxin type A was the most widely available botulinum serotype at the time and was well-known to be effective in treating pain disorders. *See, e.g.*, Ex. 1009 at 515-516; Ex. 1005A at 154; *see also* Ex. 1017 ¶69.

cl. 5	**Prior Art**
5. A method according to claim 1, wherein said toxin is administered in a dose between 1 and 30 mouse units of toxin per injection site.	*See, e.g.*, claim 1. **B&H discloses administering said toxin in a dose between 1 and 30 mouse units of toxin per injection site (*e.g.*, "1.25 units").** *See, e.g.*, Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very low ***doses of 1.25 units*** or even lower can help to break the constant spasm in this area."). *See also* Ex. 1017 ¶¶70-73.

B&H discloses Claim 5's added limitation. *See* Ex. 1017 ¶¶70-73. A POSITA would have understood that "1.25 units" disclosed in B&H is "between 1 and 30 mouse units" because a POSITA would have understood that the "units" described in B&H are "mouse units." *See* Ex. 1017 ¶72. A POSITA would have known that mouse units were the standard unit of measure for botulinum toxin and would have understood various abbreviations and synonyms for that unit of measure. *See e.g.*, Ex. 1009 at 515 ("One unit (U) corresponds to the calculated median lethal intraperitoneal dose (LD/50) in mice of the reconstituted BOTOX® inject-

ed."); *see also* Ex. 1003C; Ex. 1003D at 2; Ex. 1005A at 154; Ex. 1017 ¶72. Furthermore, the 1.25 unit dose disclosed in B&H is "a dose per injection site." *Compare* Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very ***low doses of 1.25 units or even lower***….") *with id.* ("two or three injections of 1.25 to 2.5 units ***each*** along the superior line of each trapezius."); *see also* Ex. 1017 ¶72. To the extent it is argued that any further disclosure is required, Claim 5's "dose per injection site" limitation would at minimum have been obvious to a POSITA from these express disclosures in light of the knowledge of a POSITA, who would have found it at least obvious to administer 1.25 mouse units per injection site based on B&H's disclosure of administering 1.25 units. *See* Ex. 1017 ¶73.

cl. 6	**Prior Art**
6. A method according to claim 1, wherein said toxin is administered in a single injection.	*See, e.g.*, claim 1. **B&H discloses administering said toxin through injection (*e.g.*, "[d]eep multifidus injections").** *See, e.g.*, Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very low doses of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."). *See also* Ex. 1017 ¶¶74-75.

B&H in light of the knowledge of a POSITA renders obvious Claim 6's added limitation of administering in a single injection. *See* Ex. 1017 ¶75. A POSITA reading B&H would have understood that the treatment could be carried out via a single injection, and that it would have been advantageous to do so. *See id.* A POSITA would have understood that fewer injections would minimize the

risk of complications while still maintaining efficacy. *See id.* In addition, if, as occurs, a spasm is located in only one muscle, a POSITA would have understood that a single injection could treat that spasm effectively. *See* Ex. 1005A at 151; *see also* Ex. 1017 ¶75.

cl. 7	**Prior Art**
7. A method according to claim 1, wherein said toxin is administered via a plurality of injections.	*See, e.g.*, claim 1. **B&H discloses administering said toxin via a plurality of injections (*e.g.*, "[d]eep multifidus injections").** *See, e.g.*, Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very low doses of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."). *See also* Ex.1017 ¶¶76-78.

B&H discloses Claim 7's added limitation. *See* Ex. 1017 ¶77. B&H discloses "***multifidus injections***," thus disclosing "a plurality of injections." Ex. 1003D at 2; *see also* Ex. 1017 ¶77. To the extent it is argued that any further disclosure is required, Claim 7's added limitation would at minimum have been obvious to a POSITA from these express disclosures in light of the knowledge of a POSITA, who would have found it at least obvious to administer botulinum toxin "via a plurality of injections" if a single injection was insufficient. *See* Ex. 1017 ¶78.

2. <u>Ground 3:</u> Claim 6 is obvious over B&H in view of Cheshire

a. Overview of Cheshire

Cheshire was published in *PAIN* in 1994, making it prior art to the '251 under at least §§ 102 (a) and (b). Cheshire generally discloses a method of injecting botulinum toxin A (*e.g.*, Botox® from Allergan) into trigger points in spinal muscles for the treatment of patients with myofascial pain disorders. *See* Ex. 1004; *see also* Ex. 1017 ¶¶79-80. In particular, Cheshire reports that a single and low-dose trigger point injection of botulinum toxin was effective in the treatment of certain patients. *See* Ex. 1004 at 68; *see also* Ex. 1017 ¶80.

b. Combination of the Teachings of B&H and Cheshire

As described below, a combination of the teachings of B&H and Cheshire renders obvious Claim 6 (Ground 3). *See* Ex. 1017 ¶¶79-82. A POSITA would have recognized that B&H and Cheshire are in the same field of art, both disclosing a method of botulinum toxin injection for the treatment of chronic pain syndromes involving spinal muscles. *See, e.g.*, Ex. 1003D at 1-2; Ex. 1004 at 65; Ex. 1017 ¶82. A POSITA reading B&H's disclosures of "deep multifidus injections" and the acknowledgement that "Botox" is "expensive" would have been motivated to look to Cheshire's teachings confirming that single, low-dose botulinum toxin injection can be cost-effective and efficacious in the treatment of patients with chronic myofascial pain disorders. *See, e.g.*, Ex. 1003D at 1-2; Ex. 1004 at 68; Ex. 1017 ¶82. A POSITA would have also understood that it would be advantageous to apply the single injection method taught by Cheshire in implementing the meth-

od disclosed in B&H because fewer injections would minimize the risk of complications while still maintaining efficacy. *See* Ex. 1017 ¶82. Thus, a POSITA would have been motivated to use the teachings of Cheshire in implementing the treatment method taught in B&H and would have had a reasonable expectation that the combination would work. *See id.*

c. Claim Chart for Ground 3 (Claim 6 is obvious over B&H in view of Cheshire)

cl. 6	Prior Art
6. A method according to claim 1, wherein said toxin is administered in a single injection.	*See, e.g.*, claim 1. **B&H discloses administering said toxin through injection (*e.g.*, "[d]eep multifidus injections").** *See, e.g.*, Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very low doses of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."). **Cheshire discloses administering said toxin in a single injection.** *See, e.g.*, Ex. 1004 at 68 ("Local blockade of neuromuscular transmission by ***single***, low-dose, trigger point ***injection of botulinum toxin appears to be effective*** in the treatment of some patients with chronic myofascial pain disorders affecting cervical paraspinal and shoulder girdle musculature."). *See also* Ex. 1017 ¶¶81-82.

To the extent B&H is argued not to disclose Claim 6's added limitation (as explained in Ground 2 *supra* Section V.C.1.b), it is at minimum rendered obvious by the combination of the teachings of B&H and Cheshire because Cheshire teaches that for the treatment described in B&H a "single" injection is "effective." Ex. 1017 ¶82. A POSITA would have been motivated to use Cheshire's teaching of

botulinum toxin administration in a single injection in implementing the teachings of B&H as described *supra* Section V.C.2.b.

3. <u>Ground 4:</u> Claims 1-7 are obvious over Fibromyalgia in view of B&H

a. Overview of Fibromyalgia

Like B&H, Fibromyalgia was never disclosed to the Examiner during prosecution, even though Applicant Dr. Lamb published Fibromyalgia ***on his own website*** ("www.drlamb.com"), where it was publicly available at least as of August 24, 2000, making it prior art to the '251 under at least § 102 (b). *See* Ex. 1003; 1003E; *see also* Ex. 1017 ¶83. On www.drlamb.com, Fibromyalgia was affirmatively linked to B&H through a single hyperlink labeled "Fibromyalgia." *See* Ex. 1003D. Fibromyalgia discloses, *e.g.* (Ex. 1003E at 2, 3, 6, 7; *see also* Ex. 1017 ¶84):

- Methods of treating pain disorders associated with "nerve compressions throughout the spine,"
- "disk compression and herniation,"
- "arthritis . . . of the spine," "compression arthritis," and "myofascial compression/traction neuropathy, or 'pinched nerves,'" each of which can be caused by "spastic" or "short" muscles;
- The involvement of the "deep muscles, primarily the multifidus and the rotator brevis and longus" as "the primary cause of most spinal disease";

- "Injection Therapy," including "Botox" injection, "to break the spinal and limb muscle spasm and scars."

b. Combination of the Teachings of Fibromyalgia and B&H

As described below, a combination of the teachings of Fibromyalgia and B&H renders obvious Claims 1-7 (Ground 4). A POSITA would have recognized that Fibromyalgia and B&H are in the same field of art, both describing Dr. Lamb's opinion relating to the etiology and treatment of pain syndromes involving pain from the head, neck, and back, and spinal nerve compression, and would have known that Dr. Lamb's website itself affirmatively linked these two pages discussing common topics. *See*, *e.g.*, Ex. 1003D at 1-2; Ex. 1003E at 2, 5, 6; Ex. 1017 ¶85. A POSITA reading Fibromyalgia would have been motivated to look to the teachings of B&H in order to gain a more complete understanding of Dr. Lamb's medical opinion on the pain syndromes and their treatment. Ex. 1017 ¶85. Furthermore, both Fibromyalgia and B&H teach pain treatment methods using "Botox" to relieve "spasm" in spinal muscles. *See, e.g.*, Ex. 1003D at 1-2; Ex. 1003E at 6; Ex. 1017 ¶85. While Fibromyalgia discloses that "Injection Therapy," including "Botox" injection, is a method for the treatment of disorders associated with spinal compression, that webpage does not disclose a specific protocol for such therapy. Ex. 1003E at 6. B&H, on the other hand, advantageously teaches more detailed

procedures for effectively applying "Botox" Injection Therapy to specific target muscles. Ex. 1017 ¶85. For example, B&H discloses 1.25 units or even lower doses of "Botox" by targeted injections into the multifidus muscle specifically ("Deep multifidus injections"). *See* Ex. 1003D at 2. Therefore, a POSITA reading Fibromyalgia would have been motivated to apply B&H's specific treatment procedures using known methods ("Botox" injection) in implementing the method of treating pain disorders as disclosed in Fibromyalgia. *See* Ex. 1017 ¶85. A POSITA would have had a reasonable expectation that the use of these teachings from B&H in implementing Fibromyalgia's methods would yield predictable results because B&H affirmatively discloses effective treatment for disorders associated with spinal compression similar to those disclosed in Fibromyalgia. *See* Ex. 1017 ¶85. Finally, as noted, a POSITA reading Fibromyalgia would additionally have been motivated to look to B&H because these articles were published under the same domain name (www.drlamb.com) and directly linked to each other through a single hyperlink. *See* Ex. 1017 ¶85.

c. Claim Charts for Ground 4 (Claims 1-7 are obvious over Fibromyalgia in view of B&H)

cl. 1	**Prior Art**
1. A method of treating a disorder associated	**Fibromyalgia discloses a method of treating a disorder associated with spinal compression (*e.g.*, "nerve compressions," "osteoarthritis of the joint," "disk compression and herniation," "arthritis . . . of the spine," "compression arthritis," "myofascial**

with spinal compression comprising	**compression/traction neuropathy, or 'pinched nerves,'" and "compression neuropathy").** *See, e.g.*, Ex. 1003E at 2 ("[M]ost people with fibromyalgia are suffering from diffuse muscle and tendon shortening, driven in part by multiple ***nerve compressions throughout the spine*** and limbs. … It seems ***deep spinal muscles cause deep nerve compressions*** and traction that cause further muscle problems in the spine, limbs and head."); *see also id.* ("This will cause joint ***compression of the spine*** and limbs and causes crepitus, or cracking of the joint, joint stiffness, joint pain, and eventually ***osteoarthritis of the joint***."); *id.* at 3 ("Another important principle is that muscles that remain persistently spastic or short will eventually scar into a tight spastic position causing abnormal joint movement and compression. This will lead to ***disk compression and herniation***, ***arthritis*** and subluxations ***of the spine.***"); *id.* ("This is why I have renamed osteoarthritis ***compression arthritis***, as it is a more accurate description of the cause of the arthritis."); *id.* ("Neuropathy is a term to describe nerve disease or injury. This includes diseases such as multiple sclerosis, but also includes myofascial compression/traction neuropathy, or 'pinched nerves.' The most common neuropathy, or nerve 'disease' is definitely a pinched nerve because virtually all adults and most adolescents will have some degree of ***compression neuropathy*** at the base of their neck and low back. The deep spinal muscles cause directly, or indirectly, most of the pinched nerves we experience in our lives."); *id.* at 6 ("***Some benefit can be achieved with Botox***, and, in fact, I am one of the first reported, if not the first, to treat the deepest spinal layers with Botox injection in North America."). *See also* Ex. 1017 ¶¶86-90. **B&H discloses a method of treating a disorder associated with spinal compression (*e.g.*, "nerve root irritation," "chronic headache," and "severe and chronic cervical disease in the neck").** *See* Section V.C.1.b Chart for Claim1 preamble.
[1-1] administering an effective dose of botulinum toxin	**Fibromyalgia discloses administering botulinum toxin (*e.g.*, "Botox injection").** *See, e.g.*, Ex. 1003E at 6 ("Some benefit can be achieved with ***Botox***, and, in fact, I am one of the first reported, if not the first, to treat the deepest spinal layers with ***Botox injection*** in North America."). **B&H discloses administering an effective dose (*e.g.*, "1.25 units," "successful route to get back a maximum quality of life," and**

	"help to break the constant spasm in this area, which commonly triggers the whole headache scenario") of botulinum toxin (*e.g.*, "botulinum toxin or Botox"). *See, e.g.*, Ex. 1003D at 2 ("About two years ago, we first used ***Botox*** in the deep cervical spine in hopes to release severe and chronic cervical disease in the neck. Since then, the Botox protocol we are currently using for the treatment of chronic intractable headache at the Lamb Pain Clinic is as follows-First dilute 100 units of the ***botulinum toxin or Botox*** into 4cc of non-preserved normal saline. This allows for 2.5 units in each 0.1 c.c.'s of fluid."); *id.* ("***[I]njection therapy*** with IMS and ***Botox*** can be ***a successful route to get back a maximum quality of life***."); *id.* ("Deep multifidus injections at C2 to C3 area with very low ***doses of 1.25 units*** or even lower can ***help to break the constant spasm in this area, which commonly triggers the whole headache scenario***."). *See also* Ex. 1017 ¶¶91-93.
[1-2] directly and solely to the intrinsic muscles of a patient in need of such therapy.	**Fibromyalgia discloses targeting (*e.g.*, "Botox injection") of the the intrinsic muscles (*e.g.*, "multifidus and the rotator brevis and longus muscles") of a patient in need of such therapy (*e.g.*, "thousands of my patients and myself").** *See, e.g.*, Ex. 1003E at 3 ("These ***deep muscles***, primarily the ***multifidus and the rotator brevis and longus muscles*** are probably the most important muscles of the body. … These muscles will be the primary cause of most spinal disease."); *id.* at 5 ("I have demonstrated this with thousands of my ***patients*** and myself."); *id.* at 6 ("Some benefit can be achieved with ***Botox***, and, in fact, I am one of the first reported … to treat the ***deepest spinal layers*** with ***Botox injection***"). **B&H discloses administering botulinum toxin directly and solely to the intrinsic muscles (*e.g.*, "[d]eep multifidus injections at C2 to C3 area") of a patient in need of such therapy (*e.g.*, "injection therapy . . . to get back to a maximum quality of life").** *See, e.g.*, Ex. 1003D at 2 ("First dilute 100 units of the ***botulinum toxin or Botox*** into 4cc of non-preserved normal saline. … Deep ***multifidus injections*** at C2 to C3 area with very low doses of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."); *id.* ("***[I]njection therapy*** with IMS and Botox can be a successful route ***to get back a maximum quality of life***."). *See also* Ex. 1017 ¶¶94-97.

Fibromyalgia, in view of B&H, teaches all of the limitations of Claim 1. *See* Ex. 1017 ¶¶86-97. Regarding the preamble, Fibromyalgia and B&H each independently discloses a "method of treating a disorder associated with spinal compression." B&H's disclosure is discussed *supra* Section V.C.1.b. (Claim 1 preamble); *see also* Ex. 1017 ¶90. A POSITA would have understood that Fibromyalgia discloses treatment of "nerve compressions," "osteoarthritis of the joint," "disk compression and herniation," "arthritis . . . of the spine," "compression arthritis," "myofascial compression/traction neuropathy, or 'pinched nerves,'" and "compression neuropathy," which are all "disorder[s] associated with spinal compression." *See* Ex. 1003E at 2, 3, 6; *see also* Ex. 1017 ¶87. For example, a POSITA would have understood "nerve compressions" are a type of compression neuropathy, which is a disorder associated with spinal compression. *See* Ex. 1003E at 2; Ex. 1010 at 377; Ex. 1017 ¶88. A POSITA would further have understood that Fibromyalgia expressly discloses that "osteoarthritis of the joint" is the result of "joint compression of the spine and limb," and is thus a disorder associated with spinal compression. *See* Ex. 1003E at 2; Ex. 1017 ¶89. Fibromyalgia also expressly describes that "disk compression and herniation," "arthritis . . . of the spine," and "compression arthritis" are caused by "muscles that remain persistently spastic or short [and] scar into a tight spastic position causing abnormal joint movement and compression." *See* Ex. 1003E at 3; Ex. 1017 ¶89. A POSITA would thus have

understood that these disorders are disorders associated with spinal compression and the method disclosed in Fibromyalgia is for treating these disorders by treating these shortened, tight, and spastic muscles. *See* Ex. 1017 ¶89.

Regarding Element [1-1], a POSITA would have understood that Fibromyalgia in view of B&H teaches administering an effective dose of botulinum toxin. *See* Ex. 1017 ¶91. For example, Fibromyalgia discloses that "some benefit can be achieved with Botox and, in fact, I am one of the first reported … to treat the deepest spinal layers with Botox injection." Ex. 1003E at 6. A POSITA would also have understood that B&H discloses administering an effective dose of botulinum toxin as described *supra* Section V.C.1.b. (Element [1-1]); *see also* Ex. 1017 ¶92. A POSITA would have been motivated to apply B&H's specific protocol of "Botox" injection, which includes an "effective dose" as described *supra* Section V.C.1.b., in implementing the treatment disclosed in Fibromyalgia. *See* Ex. 1017 ¶93.

Regarding Element [1-2], a POSITA would have understood from the disclosure in Fibromyalgia in view of B&H that botulinum toxin can be administered "directly and solely" to the intrinsic muscles (*e.g.*, multifidus) "of a patient in need of such therapy." *See* Ex. 1017 ¶¶94-97. For example, Fibromyalgia teaches "These deep muscles, primarily the multifidus and the rotator brevis and longus muscles are probably the most important muscles of the body. … These muscles

will be the primary cause of most spinal disease." Ex. 1003E at 3. Fibromyalgia also states "Some benefit can be achieved with Botox, and, in fact, I am one of the first reported … to treat the deepest spinal layers with Botox injection." *Id.* at 6. Furthermore, B&H discloses that botulinum toxin be administered "directly and solely" to the intrinsic muscles (*e.g.*, multifidus) of a patient in need of therapy, as described *supra* Section V.C.1.b. *See* Ex. 1017 ¶93. A POSITA reading Fibromyalgia would have found it obvious in view of the teachings of B&H to administer botulinum toxin "directly and solely" to the multifidus muscle and would have had a reasonable expectation that it would work. *See supra* Section V.C.3.b.; *see also* Ex. 1017 ¶¶95-97.

cl. 2	**Prior Art**
2. A method according to claim 1, wherein said disorder associated with spinal compression is selected from the group consisting of compression neuropathies, facet joint disease of the spin [*sic*], sciatica, disc herniation, and degenerated	*See, e.g.*, claim 1. **Fibromyalgia discloses a method of treating a disorder associated with spinal compression selected from the group consisting of compression neuropathies, facet joint disease of the spin [*sic*], sciatica, disc herniation, and degenerated discs (*e.g.*, "disk compression and herniation," "arthritis . . . of the spine," "compression arthritis," "myofascial compression/traction neuropathy, or 'pinched nerves,'" and "compression neuropathy").** *See, e.g.*, Ex. 1003E at 3 ("Another important principle is that muscles that remain persistently spastic or short will eventually scar into a tight spastic position causing abnormal joint movement and compression. This will lead to ***disk compression and herniation***, ***arthritis*** and subluxations ***of the spine.***"); *id.* ("This is why I have renamed osteoarthritis ***compression arthritis***, as it is a more accurate description of the cause of the arthritis."); *id.* ("Neuropathy is a term to describe nerve disease or injury. This includes diseases such as multiple

discs.	sclerosis, but also includes myofascial compression/traction neuropathy, or 'pinched nerves.' The most common neuropathy, or nerve 'disease' is definitely a pinched nerve because virtually all adults and most adolescents will have some degree of ***compression neuropathy*** at the base of their neck and low back. The deep spinal muscles cause directly, or indirectly, most of the pinched nerves we experience in our lives."); *id.* at 6 ("Some benefit can be achieved with ***Botox***, and, in fact, I am one of the first reported … to treat the ***deepest spinal layers*** with ***Botox injection***"). *See also* Ex. 1017 ¶¶98-101. **B&H discloses a method of treating a disorder associated with spinal compression selected from the group consisting of compression neuropathies, facet joint disease of the spin [*sic*], sciatica, disc herniation, and degenerated discs (*e.g.*, "nerve root irritation" and "severe and chronic cervical disease in the neck").** *See* Section V.C.1.b Chart for Claim 2.

For similar reasons stated above with respect to the preamble of Claim 1, Fibromyalgia and B&H (as described *supra* V.C.3.c (Claim 1 preamble)) each independently discloses Claim 2's added limitation. *See* Ex. 1017 ¶¶98-101. For example, Fibromyalgia discloses, *inter alia*, "disk compression and herniation," "compression arthritis," "myofascial compression/traction neuropathy, or 'pinched nerves,'" and "compression neuropathy." *See* Ex. 1017 ¶99. Fibromyalgia further discloses "arthritis … of the spine" which a person of ordinary skill in the art would have understood to include facet joint disease. *See e.g.*, Ex. 1007A at 7; *see also* Ex. 1017 ¶100.

cl. 3	**Prior Art**
3. A method according to	*See, e.g.*, claims 1 and 2.

claim 2, wherein the disorder is disc herniation or degenerated discs.	**Fibromyalgia discloses a method of treating a disorder such as disc herniation or degenerated discs (*e.g.*, "disk compression and herniation").** *See, e.g.*, Ex. 1003E at 3 ("Another important principle is that muscles that remain persistently spastic or short will eventually scar into a tight spastic position causing abnormal joint movement and compression. This will lead to ***disk compression and herniation***, arthritis and subluxations of the spine."); *id.* at 6 ("Some benefit can be achieved with ***Botox***, and, in fact, I am one of the first reported … to treat the ***deepest spinal layers*** with ***Botox injection***"). *See also* Ex. 1017 ¶¶102-104.

For similar reasons stated above with respect to preamble of Claim 1 and Claim 2, Fibromyalgia discloses Claim 3's added limitation, by disclosing *inter alia*, "disk compression and herniation." *See supra* Section V.C.3.c (Claim 1 preamble, Claim 2); *see also* Ex. 1017 ¶¶102-104.

cl. 4	**Prior Art**
4. A method according to claim 1, wherein said botulinum toxin paralyzing agent is botulinum toxin A.	*See, e.g.*, claim 1. **Fibromyalgia discloses a method of administering botulinum toxin A (*e.g.*, "Botox").** *See supra* discussion of **claim [1-1]**. *See also* Ex. 1017 ¶¶105-108. **B&H discloses a method of administering botulinum toxin A (*e.g.*, "Botox").** *See* Section V.C.1.b Chart for Claim 4.

Fibromyalgia and B&H (as described *supra* Section V.C.1.b (Claim 4)) each independently discloses Claim 4's added limitation. *See* Ex. 1017 ¶¶105-108. A POSITA would have understood each of Fibromyalgia and B&H's disclosures of "Botox" to refer to "botulinum toxin A" because Botox® has been a trade name for a form of botulinum toxin type A commercialized by Allergan since well before January 2002. *See e.g.*, Ex. 1009 at 515; Ex. 1003C; *see also* Ex. 1017 ¶106. To

the extent it is argued any further disclosure is required, this would at minimum have been obvious to a POSITA from these express disclosures of each of Fibromyalgia or B&H in light of the knowledge of a POSITA, who would have found it obvious to use botulinum toxin A, as claimed, because botulinum toxin type A was the most widely available botulinum serotype at the time and was well-known to be effective in treating pain disorders. *See e.g.*, Ex. 1009 at 515-516; Ex. 1005A at 154; Ex. 1004 at 65; *see also* Ex. 1017 ¶107.

cl. 5	**Prior Art**
5. A method according to claim 1, wherein said toxin is administered in a dose between 1 and 30 mouse units of toxin per injection site.	*See, e.g.*, claim 1. **B&H discloses administering said toxin in a dose between 1 and 30 mouse units of toxin per injection site (*e.g.*, "1.25 units").** *See, e.g.*, Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very low ***doses of 1.25 units*** or even lower can help to break the constant spasm in this area"). *See also* Ex. 1017 ¶¶109-112.

B&H discloses Claim 5's added limitation, as described *supra* Section V.C.1.b (Claim 5), and, to the extent it is argued any further disclosure is required, this would at minimum have been obvious to a POSITA from these express disclosures in light of the knowledge of a POSITA, for the same reasons described *supra* Section V.C.1.b (Claim 5). *See* Ex. 1017 ¶¶110-112.

cl. 6	**Prior Art**
6. A method according to claim 1, wherein said toxin is	*See, e.g.*, claim 1. **B&H discloses administering said toxin through injection (*e.g.*, "[d]eep multifidus injections").** *See, e.g.*, Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very low dos-

administered in a single injection.	es of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."). *See also* Ex. 1017 ¶¶113-115.

B&H discloses Claim 6's added limitation, as described *supra* Section V.C.1.b (Claim 6), and, to the extent it is argued any further disclosure is required, this would at minimum have been obvious to a POSITA from these express disclosures of B&H in light of the knowledge of a POSITA, for the same reasons described *supra* Section V.C.1.b (Claim 6). *See* Ex. 1017 ¶¶113-115.

cl. 7	**Prior Art**
7. A method according to claim 1, wherein said toxin is administered via a plurality of injections.	*See, e.g.*, claim 1. **B&H teaches administering said toxin via a plurality of injections (*e.g.*, "[d]eep multifidus injections").** *See, e.g.*, Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very low doses of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."). *See also* Ex. 1017 ¶¶116-119.

B&H discloses Claim 7's added limitation, as described *supra* Section V.C.1.b (Claim 7), and, to the extent it is argued any further disclosure is required, this would at minimum have been obvious to a POSITA from these express disclosures of B&H in light of the knowledge of a POSITA, for the same reasons described *supra* Section V.C.1.b (Claim 7). *See* Ex. 1017 ¶¶117-119.

4. <u>Ground 5:</u> Claim 6 is obvious over Fibromyalgia in view of B&H and Cheshire

a. Combination of the Teachings of Fibromyalgia, B&H, and Cheshire

As described below, a combination of the teachings of Fibromyalgia, B&H, and Cheshire renders obvious Claim 6 (Ground 5). *See* Ex. 1017 ¶¶120-123. A POSITA would have recognized that Fibromyalgia, B&H and Cheshire are all in the same field of art, disclosing a method of botulinum toxin injection for the treatment of chronic pain syndromes involving spinal muscles. *See, e.g.*, Ex. 1003D at 1-2; Ex. 1003E at 2, 5, 6; Ex. 1004 at 65; Ex. Ex. 1017 ¶123. Furthermore, Fibromyalgia and Cheshire both further disclose the treatment of myofascial pain. *See, e.g.*, Ex. 1003E at 3; Ex. 1004 at 65; Ex. 1017 ¶123. Fibromyalgia and B&H disclose the use of "Botox" injections for the treatment of a variety of disorders associated with spinal compression. Ex. 1003E at 2, 5, 6; Ex. 1003D at 1-2; Ex. 1017 ¶123. And B&H discloses a more specific protocol of multiple multifidus injections for referred pain from disorders associated with spinal compression. Ex. 1003D at 1-2; Ex. 1017 ¶123. When implementing the teachings of Fibromyalgia and B&H to treat a disorder associated with spinal compression, a POSITA would have understood that fewer injections would advantageously lead to a lower risk of complications. Ex. 1017 ¶123. Cheshire expressly discloses that single, low-dose botulinum toxin injection can be cost-effective and efficacious in the treatment of patients with chronic myofascial pain disorders, which a POSITA would have known are a type of disorder associated with spinal compression. *See, e.g.*, Ex. 1004 at 65; Ex. 1017 ¶123. Thus, A POSITA would have been motivated

to use the advantageous teachings of Cheshire in implementing the treatment methods of Fibromyalgia and B&H and would have had a reasonable expectation that the combination would work because Cheshire expressly discloses efficacious treatment, using a single injection of botulinum toxin A. *See* Ex. 1017 ¶123.

b. Claim Chart for Ground 5 (Claim 6 is obvious over Fibromyalgia in view of B&H and Cheshire)

cl. 6	**Prior Art**
6. A method according to claim 1, wherein said toxin is administered in a single injection.	*See, e.g.*, claim 1. **B&H discloses administering said toxin through injection (*e.g.*, "[d]eep multifidus injections").** *See, e.g.*, Ex. 1003D at 2 ("Deep multifidus injections at C2 to C3 area with very low doses of 1.25 units or even lower can help to break the constant spasm in this area, which commonly triggers the whole headache scenario."). **Cheshire discloses administering said toxin in a single injection.** *See, e.g.*, Ex. 1004 at 68 ("Local blockade of neuromuscular transmission by ***single***, low-dose, trigger point ***injection of botulinum toxin appears to be effective*** in the treatment of some patients with chronic myofascial pain disorders affecting cervical paraspinal and shoulder girdle musculature."). *See also* Ex. 1017 ¶¶121-123.

To the extent Fibromyalgia in view of B&H is argued not to disclose Claim 6's added limitation (as explained in Ground 4 *supra* Section V.C.3.c (Claim 6)), it is at minimum rendered obvious by the combination of Fibromyalgia in view of B&H and Cheshire because Cheshire teaches that a "single" injection is "effective" in implementing the teachings of Fibromyalgia and B&H. Ex. 1017 ¶122. A POSITA would have been motivated to use Cheshire's explicit teaching of botuli-

num toxin administration in a single injection in advantageously implementing the teachings of Fibromyalgia and B&H as described *supra* Section V.C.4.a.

5. Ground 6: Claims 1-4, 6, and 7 are anticipated by Travell; Ground 7: Claims 1-4, 6, and 7 are obvious over Travell in view of the knowledge of a POSITA

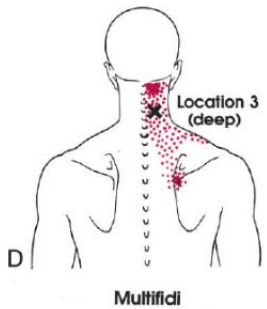
a. Overview of Travell

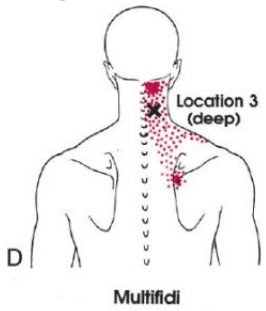
The textbook Travell was published and publicly available as of at least 1999, making it prior art to the '251 under at least §§ 102 (a) and (b). *See* Ex. 1005; Ex. 1006; Ex. 1006A; Ex. 1017 ¶¶124-125. Travell generally discloses myofascial pain syndromes referred from trigger points (TrPs) and treatment methods for releasing the TrPs. In particular, Chapter 3 of Travell describes myofascial pain referred from TrPs applicable to all muscles. *See, e.g.*, Ex. 1005A at 94 ("Considerations that apply generally to all the muscles are consolidated in this chapter."). Chapters 16 and 48 describe myofascial pain referred more specifically from TrPs in paraspinal muscles, such as multifidi and rotatores. *See, e.g.*, *id.* at 446 (Chapter 16), 916-917 (Chapter 48). To the extent it is argued these chapters from Travell do not constitute a single reference, a POSITA would certainly have been motivated and found it obvious to look to these related teachings in Chapters 3, 16 and 48 together to understand myofascial pain syndromes associated with the paraspinal muscles. *See* Ex. 1017 ¶126.

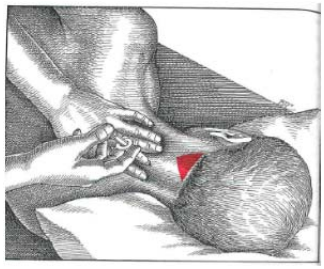
Travell discloses that increased irritability due to nerve compression (*e.g.*, spinal radiculopathy caused by a ruptured intervertebral disc) can cause development of myofascial TrPs. *See, e.g.*, Ex. 1005A at 112, 452. Travell further describes that TrPs can be found in the multifidi and rotatores muscles, located between an upper spinous process and a lower transverse process (*see, e.g.*, *id.* at 455, 466), and can be released with botulinum toxin A injections (*see, e.g.*, *id.* at 150, 154-155, 466). Travell also reviews earlier literature, including Cheshire, where botulinum toxin A injections were reported to be effective in treating myofascial TrPs. *Id.* at 155, 174. Travell further discloses that "[i]t is important when using BTA to inject the minimum amount necessary and ***only in the TrP***, since BTA destroys normal and dysfunctional TrP endplates alike." *Id.* at 155. Travell further discloses that "it is much better to inject *small* amounts *precisely* where the contraction knots of the TrP are located" and further that "[o]ne well-performed injection can fully inactivate a TrP immediately." *Id.* at 150-151. *See, generally* Ex. 1017 ¶127.

b. Claim Charts for Ground 6 (Claims 1-4, 6, and 7 are anticipated by Travell) and Ground 7 (Claims 1-4, 6, and 7 are obvious over Travell in view of the knowledge of a POSITA)

cl. 1	**Prior Art**
1. A method of treating a disorder associated	**Travell discloses a method of treating a disorder associated with spinal compression (*e.g.*, "nerve compression," "radiculopathy," "ruptured intervertebral disc," "nerve irritabil-**

with spinal compression comprising	**ity," "hypomobile cervical-occipital junction," "ruptured disc," and "disc herniation").** *See, e.g.*, Ex. 1005A at 112 ("***Nerve compression***, such as in the ***radiculopathy*** caused by a ***ruptured intervertebral disc***, favors the development of TrPs in the muscles supplied by the compressed nerve root (postdisc syndrome). Less severe radiculopathy also can activate TrPs."); *id.* at 452 ("Neuropathy. Increased ***nerve irritability due to entrapment***, as in ***spinal radiculopathy***, can be a significant factor in the activation and perpetuation of these posterior cervical TrPs. A comparable response has been well documented for lumbar paraspinal muscles."); *id.* at 459 ("Neuropathy. Clinically, ***cervical radiculopathy*** can activate TrPs in the posterior cervical muscles that, following surgery, are then perpetuated by other factors. … Cervical radiculopathy is much more likely to show a positive Sperling test, pain elicited by ***spinal compression*** applied as downward pressure on the head with the upright cervical spine slightly extended. … The strong relation between lumbar radiculopathy and TrPs in lumbar paraspinal muscles was recently demonstrated by Chu."); *id.* at 467 ("In one patient with ***a chronically locked hypomobile cervical-occipital junction*** who was receiving osteopathic manipulation, injection of the cervical multifidi and rotatores bilaterally increased left lateral rotation 45º to reach full range of motion"); *id.* at 924 ("The ***rupture of an intervertebral disc***, ligamentous strain, and paraspinal muscular overload that activates myofascial TrPs are all likely to be caused by similar strains."); *id.* at 925 ("Radiculopathy may be caused by pressure from a ***ruptured disc***, by encroachment within the spinal foramen as from osteoarthritis, or by a tumor."); *id.*("an L_4-L_5 lateral ***disc herniation*** produces tightness of the left L_4-L_5 multifidus muscle, causing a segmental motion block."); *id.* at 466 ("Location 3 of Figure 16.1A and D illustrates a common location and pain pattern of ***TrPs in the multifidus***. When ***injecting this TrP***, to reach it one must penetrate several layers of muscle …"); *id.* at Fig. 16.1D:  *Id.* at 164 ("Recently activated (acute) myofascial TrPs that have no perpetuating factors or additional tissue damage because of mechanical injury to other tissues (i.e.,

	TrPs that are uncomplicated) should resolve with one or two injections."). *See also* Ex. 1017 ¶¶128-130.
[1-1] administering an effective dose of botulinum toxin	**Travell discloses administering an effective dose (*e.g.*, "clinically effective" and "effective therapeutic agent") of botulinum toxin (*e.g.*, "Botulinum toxin type A (BTA)").** *See, e.g.*, Ex. 1005A at 154 ("***Botulinum toxin*** type A (BTA)"); *id.* at 155 ("***BTA injection*** for the treatment of myofascial TrPs has been reported by several authors to be clinically ***effective***.[2, 30, 192]"); *see also id.* at 174 ("30. Cheshire WP, Abashian SW, Mann JD: Botulinum toxin in the treatment of myofascial pain syndrome. *Pain* 59:65-59, 1994"); *id.* at 155 ("One randomized, double-blind, placebo-controlled study in 6 subjects compared the effect of TrP injections into cervical paraspinal and shoulder girdle muscles. Four patients experienced at least 30% reduction in TrP symptoms and signs following BTA but not saline injection … This study strengthens the expectation that ***BTA would be an effective therapeutic agent for injecting TrPs***."). *See also* Ex. 1017 ¶¶131-133.
[1-2] directly and solely to the intrinsic muscles of a patient in need of such therapy.	**Travell discloses administering botulinum toxin directly and solely (*e.g.*, "only in the TrP" and "only where endplates were located") to the intrinsic muscles (*e.g.*, multifidi, and rotatores muscles) of a patient in need of such therapy (*e.g.*, Figs. 16.1D and 16.9).** *See, e.g.*, Ex. 1005A at 155 ("It is important when using ***BTA to inject*** the minimum amount necessary and ***only in the TrP***, since BTA destroys normal and dysfunctional TrP endplates alike. Ottaviani and Childers emphasized the importance of ***injecting BTA only where endplates were located*** …"); *id.* at 466 ("Location 3 of Figure 16.1A and D illustrates a common location and pain pattern of ***TrPs in the multifidus***. When ***injecting this TrP***, to reach it one must penetrate several layers of muscle …"); *id.* at Fig. 16.1D:  *Id.* at 164 ("Recently activated (acute) myofascial TrPs that have no perpetuating factors or additional tissue damage because of mechanical injury to other tissues (i.e., TrPs that are uncomplicated) should

	resolve with ***one*** or two injections."); *id.* at 150 ("The number of injections should be counted in terms of ***the number of TrP sites injected***, not the number of times some solution has been deposited within one TrP site."); *id* at 150-51 ("Some clinicians depend on the injection of large amounts of seriously myotoxic drugs like Botulinum toxin A … [but] it is much better to inject ***small amounts precisely where the contraction knots of the TrP are located***."); *id* at 151 ("Success [of injection] depends strongly on the accuracy of the clinician's aim. This accuracy depends strongly on the precision with which the TrP was localized and the skill of the clinician."); *id.* at Figure 16.9 ("Injection of the location in the left posterior cervical muscles near the C_4 level where one may encounter ***trigger points of*** the middle semispinalis capitis, semispinalis cervicis, ***multifidi, and rotatores muscles***.")  *See also* Ex. 1017 ¶¶134-138.

Travell discloses all of the limitations of Claim 1. *See* Ex. 1017 ¶¶128-138. Regarding the preamble, Travell discloses a method of treating "nerve compression," "radiculopathy," "ruptured intervertebral disc," "nerve irritability," "hypomobile cervical-occipital junction," "ruptured disc," and "disc herniation," which are all "disorder[s] associated with spinal compression." *See* Ex. 1017 ¶128. For example, Travell discloses that trigger points, which cause myofascial pain (*see* Ex. 1005A at 95), can be developed and activated as a symptom of nerve compression (*see id.* at 112), radiculopathy (*see id.* at 452) or ruptured intervertebral disc (*see id.* at 924). Travell teaches that the trigger points can be resolved with the injection method it describes. *See, e.g., id.* at 164. Furthermore, Travell discloses that a pa-

tient with a chronically locked hypomobile cervical-occipital junction showed improved mobility after receiving the treatment disclosed in Travell. *See id.* at 467. *See also* Ex. 1017 ¶¶128-129.

To the extent it is argued any further disclosure is required to meet the preamble, the preamble would at minimum have been obvious to a POSITA from the disclosures of Travell in light of the knowledge of a POSITA, who would know to apply the method disclosed in Travell to treat a disorder associated with spinal compression. This would have been obvious especially because, among other things, disorders associated with spinal compression were well known to involve pathophysiological changes in the muscles (*e.g.*, development of TrPs), similar to myofascial pain treated in Travell and thus would have been reasonably expected to respond to similar treatment. *See* Ex. 1017 ¶130.

Regarding Element [1-1], Travell discloses administering an effective dose of botulinum toxin because Travell expressly discloses botulinum toxin injection methods that were clinically "effective." *See, e.g.*, Ex. 1005A at 155, 174; Ex. 1017 ¶¶131-132. At minimum, in light of these disclosures, this limitation would have been obvious to a POSITA, who would have found it obvious to use a dose that would be effective to treat the disorder, in implementing the method disclosed in Travell. *See* Ex. 1017 ¶133.

Regarding Element [1-2], Travell discloses a method involving botulinum toxin injection "directly and solely" to the intrinsic muscles (*e.g.*, multifidus and rotatores) of "a patient in need of such therapy." For example, Travell expressly discloses a method of injection directly targeted into trigger points located in the multifidi and rotatores muscles (*see* Ex. 1005A at Figs. 16.1D and 16.9) and further discloses that botulinum toxin injection should be "only in the TrP, since BTA destroys normal and dysfunctional TrP endplates alike" (*see, e.g., id.* at 155) and that "it is much better to inject small amounts precisely where the contraction knots of the TrP are located" (*see, e.g., id.* at 150-151). Thus, Travell expressly discloses administering botulinum toxin straight into the intrinsic muscles and only the intrinsic muscles in a manner that would minimize diffusion of the toxin into surrounding tissue. *See* 1017 ¶¶134-135.

Even if the term "directly and solely" is construed narrowly to require administration only to the intrinsic muscles (and not to other muscle groups) during a given treatment session, Travell discloses this limitation. For example, Travell discloses that acute myofascial TrPs can be resolved with a single injection (*see, e.g.*, Ex. 1005A at 164), which is further explained to mean injecting into a single TrP site (*see, e.g., id.* at 150). *See* 1017 ¶136. To the extent it is argued that further disclosure is required with respect to this element, a POSITA would, at minimum, have been motivated and found it obvious based on these teachings of Trav-

ell to administer botulinum toxin "directly and solely" to the intrinsic muscles, whichever construction is applied. For example, a POSITA would have been motivated and found it obvious to administer botulinum toxin straight into the muscles in a manner that minimizes diffusion to reduce the risk of potential side effects (*see, e.g.*, Ex. 1005A at 155; Ex. 1004 at 66) and to save the expensive botulinum toxin (*see, e.g.*, Ex. 1003D at 2; Ex. 1003C at 1). *See* 1017 ¶137. Moreover, a POSITA would have been motivated and found it obvious to administer only to the intrinsic muscles (and not to other muscle groups) in order to specifically target the source of a given disorder (when a TrP is located in the intrinsic muscles) and to limit unnecessary treatments. *See* 1017 ¶138. A POSITA would have had a reasonable expectation that such specific administration methods would work. *See, e.g.*, Ex. 1005A at 150-151, 164, 467; *see also* Ex. 1017 ¶¶137-138.

cl. 2	**Prior Art**
2. A method according to claim 1, wherein said disorder associated with spinal compression is selected from the group consisting of compression neuropathies, facet joint disease of the spin [*sic*], sciatica,	*See, e.g.*, claim 1. **Travell discloses a method of treating a disorder associated with spinal compression selected from the group consisting of compression neuropathies, facet joint disease of the spin [*sic*], sciatica, disc herniation, and degenerated discs (*e.g.*, "nerve compression," "radiculopathy," "ruptured intervertebral disc," "nerve irritability," "hypomobile cervical-occipital junction," "ruptured disc," and "disc herniation").** *See, e.g.*, Ex. 1005A at 112 ("***Nerve compression***, such as in the ***radiculopathy*** caused by a ***ruptured intervertebral disc***, favors the development of TrPs in the muscles supplied by the compressed nerve root (postdisc syndrome). Less severe

disc herniation, and degenerated discs.	radiculopathy also can activate TrPs."); *id.* at 452 ("Neuropathy. Increased ***nerve irritability due to entrapment***, as in ***spinal radiculopathy***, can be a significant factor in the activation and perpetuation of these posterior cervical TrPs. A comparable response has been well documented for lumbar paraspinal muscles."); *id.* at 459 ("***Neuropathy*** Clinically, ***cervical radiculopathy*** can activate TrPs in the posterior cervical muscles that, following surgery, are then perpetuated by other factors. … Cervical radiculopathy is much more likely to show a positive Sperling test, pain elicited by ***spinal compression*** applied as downward pressure on the head with the upright cervical spine slightly extended."); *id.* at 467 ("In one patient with ***a chronically locked hypomobile cervical-occipital junction*** who was receiving osteopathic manipulation, injection of the cervical multifidi and rotatores bilaterally increased left lateral rotation 45º to reach full range of motion"); *id.* at 924 ("The ***rupture of an intervertebral disc***, ligamentous strain, and paraspinal muscular overload that activates myofascial TrPs are all likely to be caused by similar strains."); *id.* at 925 ("Radiculopathy may be caused by pressure from a ***ruptured disc***, by encroachment within the spinal foramen as from osteoarthritis, or by a tumor."); *id.*("an L_4-L_5 lateral ***disc herniation*** produces tightness of the left L_4-L_5 multifidus muscle, causing a segmental motion block."). *See also* Ex. 1017 ¶¶ 139-146.

For similar reasons stated above with respect to the preamble of Claim 1, Travell discloses Claim 2's added limitation by disclosing, *inter alia*, "nerve compression" (Ex. 1005A at 112), "radiculopathy" (*id.*), "ruptured intervertebral disc" (*id.*), "nerve irritability" (*id.* at 452), "hypomobile cervical-occipital junction" (*id.* at 467), "ruptured disc" (*id.* at 925), and "disc herniation" (*id.*). *See also* Ex. 1017 ¶¶140-145. To the extent it is argued any further disclosure is required, Claim 2's added limitation would have at minimum been obvious to a POSITA from these express disclosures in light of the knowledge of a POSITA, for the reasons described above in the discussion of the preamble of Claim 1. *See* Ex. 1017 ¶146.

cl. 3	**Prior Art**
3. A method according to claim 2, wherein the disorder is disc herniation or degenerated discs.	*See, e.g.*, claims 1 and 2. **Travell discloses a method of treating a disorder such as disc herniation or degenerated discs (*e.g.*, "ruptured intervertebral disc," "ruptured disc," and "disc herniation").** *See, e.g.*, Ex. 1005A at 112 ("Nerve compression, such as in the radiculopathy caused by a ***ruptured intervertebral disc***, favors the development of TrPs in the muscles supplied by the compressed nerve root (postdisc syndrome). Less severe radiculopathy also can activate TrPs."); *id.* at 924 ("The ***rupture of an intervertebral disc***, ligamentous strain, and paraspinal muscular overload that activates myofascial TrPs are all likely to be caused by similar strains."); *id.* at 925 ("Radiculopathy may be caused by pressure from a ***ruptured disc***, by encroachment within the spinal foramen as from osteoarthritis, or by a tumor."); *id.*("an L_4-L_5 lateral ***disc herniation*** produces tightness of the left L_4-L_5 multifidus muscle, causing a segmental motion block."). *See also* Ex. 1017 ¶¶147-150.

For similar reasons stated above with respect to the preamble of Claims 1 and 2, Travell discloses Claim 3's added limitation by disclosing, *inter alia*, "ruptured disc" and "disc herniation." *See* Ex. 1017 ¶¶148-149. To the extent it is argued any further disclosure is required, Claim 3's added limitation would at minimum have been obvious to a POSITA from these express disclosures in light of the knowledge of a POSITA, for the reasons described above in the discussion of the preamble of Claim 1 and Claim 2. *See* Ex. 1017 ¶150.

cl. 4	**Prior Art**
4. A method according to claim 1, wherein said botulinum toxin paralyzing agent is botulinum toxin A.	*See, e.g.,* claim 1. **Travell discloses a method of administering botulinum toxin A (*e.g.*, "Botulinum toxin type A (BTA)").** *See, e.g.*, Ex. 1005A at 154 ("***Botulinum toxin type A (BTA)***"); *id.* at 155 ("***BTA injection*** for the treatment of myofascial TrPs has been reported by several authors to be clinically effective."). *See also* Ex. 1017 ¶¶151-153.

Travell discloses the additional limitation of Claim 4 or at minimum renders it obvious in view of the knowledge of a POSITA, who would have found it obvious to use botulinum toxin A in implementing the method disclosed in Travell, because botulinum toxin type A was the most widely available botulinum serotype at the time and was well-known to be effective in treating pain disorders. *See e.g.*, Ex. 1009 at 515-516; Ex. 1005A at 154; Ex. 1004 at 65; *see also* Ex. 1017 ¶153.

cl. 6	**Prior Art**
6. A method	*See, e.g.*, claim 1.

according to claim 1, wherein said toxin is administered in a single injection.	**Travell discloses administering said toxin in a single injection (*e.g.*, "one … injection[]" and "One well-performed injection").** *See, e.g.*, Ex. 1005A at 164 ("Recently activated (acute) myofascial TrPs that have no perpetuating factors or additional tissue damage because of mechanical injury to other tissues (i.e., TrPs that are uncomplicated) should resolve with ***one*** or two injections."); *id.* at 151 ("***One well-performed injection*** can fully inactivate a TrP immediately"). Ex. 1017 ¶¶154-156.

Travell discloses Claim 6's added limitation or at minimum renders it obvious in view of the knowledge of a POSITA, who would have understood that it would be advantageous to administer botulinum toxin "in a single injection" in implementing the method disclosed in Travell because fewer injections would minimize the risk of complications while still maintaining efficacy. *See* Ex. 1017 ¶¶155-156.

cl. 7	**Prior Art**
7. A method according to claim 1, wherein said toxin is administered via a plurality of injections.	*See, e.g.*, claim 1. **Travell discloses administering said toxin via a plurality of injections (*e.g.*, "two injections").** *See, e.g.*, Ex. 1005A at 164 ("Recently activated (acute) myofascial TrPs that have no perpetuating factors or additional tissue damage because of mechanical injury to other tissues (i.e., TrPs that are uncomplicated) should resolve with one or ***two injections***."). *See also* Ex. 1017 ¶¶157-159.

Travell discloses Claim 7's added limitation or at minimum renders it obvious in view of the knowledge of a POSITA, who would have found it at least obvious to administer botulinum toxin "via a plurality of injections" if a single injection was insufficient. *See* Ex. 1017 ¶¶158-159.

6. Ground 8: Claim 5 is obvious over Travell in view of Cheshire

a. Combination of the Teachings of Travell and Cheshire

As described below, a combination of the teachings of Travell and Cheshire renders obvious Claim 5 (Ground 8). *See* Ex. 1017 ¶¶160-164. A POSITA would have recognized that Travell and Cheshire are in the same field of art, both disclosing a method of botulinum toxin injection for the treatment of myofascial pain syndromes involving paraspinal muscles. *See, e.g.*, Ex. 1005A at 150, 154-55, 455; Ex. 1004 at 65. Furthermore, Travell specifically cites Cheshire, stating that "BTA injection for the treatment of myofascial TrPs has been reported by several authors to be clinically effective." Ex. 1005A at 155, 174. Thus, a POSITA reading Travell would have been motivated to look to Cheshire's teachings in order to learn a specific way of administering botulinum toxin A that was found effective. A POSITA would have known that Cheshire expressly identifies a specific dose of botulinum toxin A that was effective to treat myofascial pain. Ex. 1004 at 68 ("a total dose of 50 mouse units of botulinum toxin … divided equally among 2 or 3 sites.") Thus, a POSITA would have been motivated to apply teachings of Cheshire in implementing Travell and would have had a reasonable expectation that such application would work. *See generally* Ex. 1017 ¶164.

b. Claim Chart for Ground 8 (Claim 5 is obvious over Travell in view of Cheshire)

cl. 5	Prior Art
5. A method according to claim 1, wherein said toxin is administered in a dose between 1 and 30 mouse units of toxin per injection site.	*See, e.g.*, claim 1. **Cheshire, which is referenced in Travell, discloses administering said toxin in a dose between 1 and 30 mouse units of toxin per injection site (*e.g.*, "a total dose of 50 mouse units of botulinum toxin in 4ml normal saline divided equally among 2 or 3 sites").** *See, e.g.*, Ex. 1005A at 155 ("BTA injection for the treatment of myofascial TrPs has been reported by several authors to be clinically effective.[2, 30, 192]"); *see also id.* at 174 ("30. Cheshire WP, Abashian SW, Mann JD: Botulinum toxin in the treatment of myofascial pain syndrome. *Pain* 59:65-59, 1994"); Ex. 1004 at 67 ("Trigger points were injected with ***a total dose of 50 mouse units of botulinum toxin*** in 4ml normal saline ***divided equally among 2 or 3 sites***."). *See also* Ex. 1017 ¶¶160-164.

Cheshire discloses the additional limitation in Claim 5. *See* Ex. 1017 ¶¶162-164. A POSITA would have known that "a total dose of 50 mouse units . . . divided equally among 2 or 3 sites" is approximately 16.67 mouse units (3 sites) or 25 mouse units (2 sites) per injection site. A POSITA would have been motivated and found it obvious to use Cheshire's teaching of a specific dose of botulinum toxin in implementing the method of Travell as described *supra* Section V.C.6.a. *See also* Ex. 1017 ¶164.

* * *

For all of the grounds discussed herein, to the extent it is argued that any further disclosure is required for a limitation in the Challenged Claims identified herein as having been disclosed (explicitly or inherently), a POSITA would certainly

have found that limitation obvious to include based on the same disclosures and analysis identified herein.

VI. CONCLUSION

Because this Petition, if unrebutted, shows that there is a reasonable likelihood that these claims are unpatentable, Petitioners request this Petition be instituted and the Challenged Claims be found unpatentable and canceled. Per §§ 1.33(c), 42.105, and 42.100, a copy of the present Request, in its entirety, is being served on the Patent Owner at the address of record as reflected in the publicly available records of the PTO as designated in the PAIR system. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this proceeding by this firm) to Deposit Account 18-1945, under Order No. 111682-0002-651.

Respectfully submitted by: /J. Steven Baughman/ October 28, 2015

J. Steven Baughman (lead counsel)
Reg. No. 47,414
steven.baughman@ropesgray.com
Megan Raymond (backup counsel)
Reg. No. 72,997
megan.raymond@ropesgray.com
ROPES & GRAY LLP
2099 Pennsylvania Avenue, NW
Washington, DC 20006-6807
P: 202-508-4606 / F: 202-383-8371

Andrew N. Thomases (backup counsel)
Reg. No. 40,841
andrew.thomases@ropesgray.com
ROPES & GRAY LLP
1900 University Avenue, 6th Floor
East Palo Alto, CA 94303
P: 650-617-4712 / F: 650-566-4275

Mailing address for all PTAB correspondence: **ROPES & GRAY LLP**
IPRM – Floor 43, Prudential Tower, 800 Boylston Street, Boston, MA 02199-3600

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

United States Patent No.: 6,806,251	§	Attorney Docket No.:
Inventor: Gregory Blair Lamb	§	111682-0002-651
Formerly Application No.: 10/062,954	§	Customer No. 28120
Issue Date: Oct. 19, 2004	§	
Filing Date: Jan. 31, 2002	§	Petitioners: Allergan, Inc.;
Former Group Art Unit: 1648	§	Allergan Sales, LLC
Former Examiners: J. Housel; Z. Lucas	§	
	§	

For: METHOD OF TREATING PAIN

MAIL STOP PATENT BOARD
Patent Trial and Appeal Board
United States Patent and Trademark Office
Post Office Box 1450
Alexandria, Virginia 22313-1450

PETITION FOR *INTER PARTES* REVIEW OF UNITED STATES PATENT NO. 6,806,251

CERTIFICATE OF SERVICE

It is certified that a copy of the following documents has been served in its entirety on the patent owner as provided in 37 CFR § 42.205:

1. Petition For *Inter Partes* Review of United States Patent No. 6,806,251 Pursuant to 35 U.S.C. § 321, 37 C.F.R. § 42.304 and accompanying exhibits:

Exhibit	Description
Ex.1001	U.S. Patent No. 6,806,251
Ex.1002	File History of U.S. Patent No. 6,806,251

Ex. 1003	Declaration of Christopher Butler
Ex. 1003A	Exhibit A to the Declaration of Christopher Butler – Lamb, "DrLamb.com" (Oct. 18, 2000 archive of http://www.drlamb.com/)
Ex. 1003B	Exhibit B to the Declaration of Christopher Butler – Lamb, "Pain Topics" (Oct. 14, 2000 archive of http://drlamb.com/PainTopics.htm)
Ex. 1003C	Exhibit C to the Declaration of Christopher Butler – Lamb, "The Magic of Botox" (Oct. 28, 2000 archive of http://www.drlamb.com/magicbotox.htm)
Ex.1003D	Exhibit D to the Declaration of Christopher Butler – Lamb, "Botox and IMS for Intractable Headache" (Jan. 19, 2001 archive of http://drlamb.com/botoxheadaches.htm) ("B&H")
Ex.1003E	Exhibit E to the Declaration of Christopher Butler – Lamb, "Is There a Cure for Fibromyalgia?" (Oct. 19, 2000 archive of http://www.drlamb.com/curefibromyalgia.htm) ("Fibromyalgia")
Ex. 1003F	Exhibit F to the Declaration of Christopher Butler – Lamb, "Acupuncture For Pain Relief Puncture Accurately" (Oct. 12, 2000 archive of http://drlamb.com/Accupuncture.htm)
Ex. 1003G	Exhibit G to the Declaration of Christopher Butler – Lamb, "Ask Dr. Lamb" (Oct. 16, 2000 archive of http://drlamb.com/secondopinion.htm)
Ex. 1003H	Exhibit H to the Declaration of Christopher Butler – Lamb, "DrLamb.com" (Feb. 26, 2001 archive of http://www.drlamb.com/)
Ex. 1003I	Exhibit I to the Declaration of Christopher Butler – Lamb, "Pain Topics" (Feb. 5, 2001 archive of http://drlamb.com/PainTopics.htm)
Ex. 1003J	Exhibit J to the Declaration of Christopher Butler – Lamb, "The Magic of Botox" (Feb. 16, 2001 archive of http://www.drlamb.com/magicbotox.htm)
Ex. 1003K	Exhibit K to the Declaration of Christopher Butler – Lamb, "Botox and IMS for Intractable Headache" (Feb. 22, 2001 archive of http://drlamb.com/botoxheadaches.htm)
Ex. 1003L	Exhibit L to the Declaration of Christopher Butler – Lamb, "Is There a Cure for Fibromyalgia?" (Feb. 14, 2001 archive of http://www.drlamb.com/curefibromyalgia.htm)
Ex. 1003M	Exhibit M to the Declaration of Christopher Butler – Lamb, "Acupuncture For Pain Relief Puncture Accurately" (Feb. 17, 2001 archive of http://drlamb.com/Accupuncture.htm)
Ex. 1003N	Exhibit N to the Declaration of Christopher Butler – Lamb, "Ask Dr. Lamb" (Feb. 19, 2001 archive of http://drlamb.com/secondopinion.htm)

Ex. 1004	Cheshire *et al.*, "Botulinum toxin in the treatment of myofascial pain syndrome," PAIN 59, 65-69 (1994) ("Cheshire")
Ex. 1005	Declaration of Jacqueline Lewis
Ex. 1005A	Exhibit A to the Declaration of Jacqueline Lewis – Simons *et al.*, *Travell & Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual Volume 1. Upper Half of Body* (2d ed. 1999) ("Travell")
Ex. 1006	Certification of Sally Jennings
Ex. 1006A	Exhibit A to the Certification of Sally Jennings – excerpts from the Travell textbook
Ex. 1007	Declaration of Hayan Yoon
Ex. 1007A	Exhibit A to the Declaration of Hayan Yoon – Gunn, *The Gunn Approach to the Treatment of Chronic Pain: Intramuscular Stimulation for Myofascial Pain of Radiculopathic Origin* (2d ed. 1996) ("Gunn")
Ex. 1008	Declaration of Deborah Rae
Ex. 1008A	Exhibit A to the Declaration of Deborah Rae – excerpts from the Gunn textbook
Ex. 1008B	Exhibit B to the Declaration of Deborah Rae – the electronic record of a copy of the Gunn textbook cataloged in the University of Delaware Library
Ex. 1009	Physicians' Desk Reference (55th ed. 2001), Medical Economics
Ex. 1010	Mosby's Medical, Nursing & Allied Health Dictionary (5th ed. 1998), A Time Mirror Company
Ex. 1011	International Publication No. WO 94/15629 filed by Borodic ("Borodic")
Ex. 1012	Guyer, "Mechanism of Botulinum Toxin in the Relief of Chronic Pain," CURRENT REVIEW OF PAIN, 3:427-431 (1999) ("Guyer")
Ex. 1013	Bogduk, "Cervicogenic Headache: Anatomic Basis and Pathophysiologic Mechanisms," CURRENT REVIEW OF PAIN, 5:382-386 (2001) ("Bodguk")
Ex. 1014	Jansen, "Surgical treatment of non-responsive cervicogenic headache," CLIN. EXP. RHEUMATOL, 18:S67-S70 (2000) ("Jansen")
Ex. 1015	Sheldon, "Headache Patterns and Cervical Nerve Root Compression – A 15-Year Study of Hospitalization For Headache," HEADACHE 6(4):180-188 (1967) ("Sheldon")
Ex. 1016	Allergan's Answer (D.I. 30, dated July 30, 2015), *1474791 Ontario, Ltd. v. Allergan, Inc., et al.*, Case No. 1:15-cv-03372 (N.D. Ill.)
Ex. 1017	Declaration of Edgar Ross

Ex. 1018	Declaration of Richard Moncrief
Ex. 1019	Certification of Sally Jennings

The copy has been served on October 28, 2015 by causing the aforementioned documents to be deposited in the United States Postal Service as Express Mail postage pre-paid in an envelope addressed to:

Correspondence Address:	Additon, Higgins & Pendleton, P.A. 11610 North Community House Road, Suite 200 Charlotte, NC 28277-2199 Express Mail: EF 070 060 791 US
Litigation Counsel:	Joseph Cwik Shashank Upadhye AMIN TALATI & UPADHYE, LLC 55 West Monroe Street, Suite 3400 Chicago, IL 60603 Express Mail: EF 070 060 805 US

Dated: October 28, 2015

ROPES & GRAY LLP

/s/ Kerstyn Crumb
Kerstyn Crumb