Filed: July 19, 2016

Filed on behalf of:
ULTHERA, INC.
By: John B. Sganga, Jr.
Matthew S. Bellinger
Michelle E. Armond
KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 Main Street, 14th Floor
Irvine, CA 92614
Ph.: (949) 760-0404 Fax: (949) 760-9502
E-mail: BoxUlthera@knobbe.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ULTHERA, INC.,
Petitioner

v.

DERMAFOCUS LLC,
Patent Owner

Case No. TBD
Patent 6,113,559

PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 6,113,559

TABLE OF CONTENTS

Page No.

TABLE OF CONTENTS
(*cont'd*)

Page No.

TABLE OF CONTENTS
(*cont'd*)

Page No.

TABLE OF AUTHORITIES

Page No(s).

OTHER AUTHORITIES

TABLE OF AUTHORITIES
(*cont'd*)

Page No(s).

EXHIBIT LIST

Exhibit No.	Description
1001	U.S. Patent No. 6,113,559 to Klopotek ("the '559 patent")
1002	'559 patent file history
1003	Declaration of Mark E. Schafer, Ph.D.
1004	Curriculum Vitae of Mark E. Schafer, Ph.D.
1005	International PCT Publication WO96/34568 ("Knowlton")
1006	French Patent No. 2,672,486 ("Technomed patent")
1007	English translation of Technomed patent (Ex. 1006)
1008	International PCT Publication WO93/12742 ("Technomed PCT")
1009	English translation of Technomed PCT (Ex. 1008)
1010	U.S. Patent No. 5,601,526, which claims priority to Technomed PCT
1011	File history for European Patent Application No. 98964890.2
1012	Translator Declaration
1013	U.S. Patent No. 5,230,334 to Klopotek
1014	U.S. Patent No. 5,755,753 to Knowlton
1015	Excerpts from The American Medical Association Encyclopedia of Medicine (1989)
1016	The Simultaneous Study of Light Emissions and Shock Waves Produced by Cavitation Bubbles, G. Gimenez, *J. Acoust. Soc. Am.* 71(4), April 1982, pp.839-847

Exhibit No.	Description
1017	Excerpts from Gray's Anatomy (1995)
1018	Anatomy of the Superficial Venous System, Comjen G.M., *Dermatol. Surg.*, 1995; 21:35-45
1019	Section 2.6 from *Ultrasonics Theory and Application*, by G.L. Gooberman (Hart Publishing Co., 1969)
1020	Deep Local Hyperthermia for Cancer Therapy: External Electromagnetic and Ultrasound Techniques, A.Y. Cheung and A. Neyzari, *Cancer Research* (Suppl.), Vol. 44, pp. 4736-4744 (1984)

Petitioner Ulthera, Inc. ("Ulthera") requests *inter partes* review in accordance with 35 U.S.C. §§ 311-319 and 37 C.F.R. § 42.100 *et seq.* of Claims 1-18 of U.S. Patent No. 6,113,559 ("the '559 patent") which issued on September 5, 2000, and is now purportedly owned by DermaFocus LLC ("DermaFocus").

I. INTRODUCTION

Ulthera is a leading innovator of ultrasound technology for medical and aesthetic applications. Ulthera's products include its successful Ultherapy® System, which Ulthera has sold in the U.S. since 2009 and invested substantial time and resources developing. The Ultherapy® System uses ultrasound energy to non-invasively lift and tighten a patient's skin, in areas such as the face or neck. The Ultherapy® System was the first energy-based device to receive U.S. Food and Drug Administration clearance for a non-invasive aesthetic lift indication.

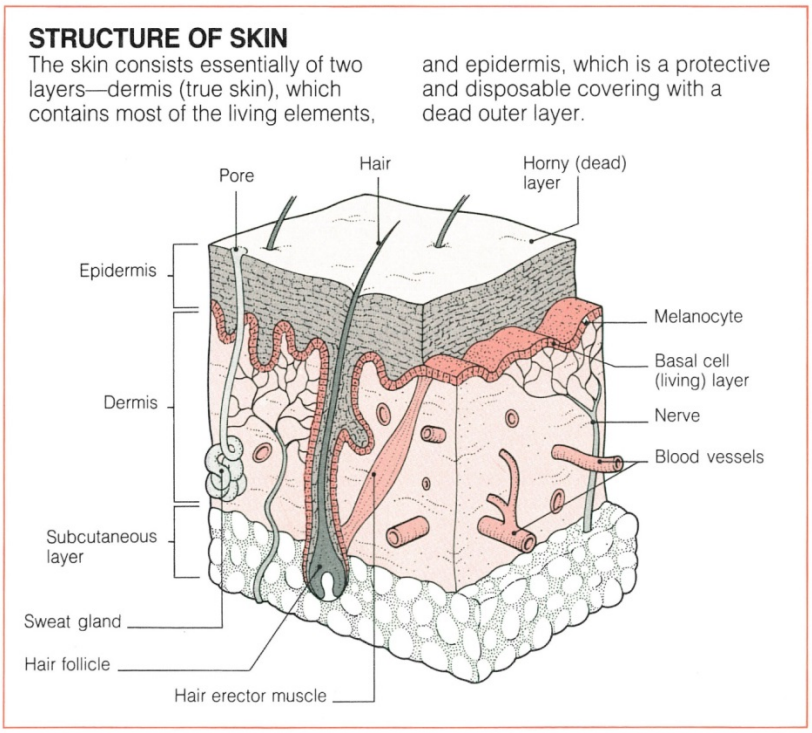
DermaFocus is a non-practicing entity and the purported owner of the '559 patent. Ulthera is unaware of any commercial devices marketed or sold by DermaFocus or by any prior owners of the '559 patent. Ulthera is also unaware of any instances in which the '559 patent was licensed to third-parties or of any prior attempts to enforce the patent.

DermaFocus sued Ulthera for alleged infringement of the '559 patent on July 29, 2015, two weeks after DermaFocus was formed and allegedly obtained ownership of the patent and approximately six years after Ulthera commercially

launched the accused Ultherapy® System. *See DermaFocus LLC v. Ulthera, Inc.*, No. 1:15-CV-00654-SLR (D. Del.). Prior to filing that lawsuit, neither DermaFocus nor any prior owner contacted Ulthera about any alleged infringement of the ’559 patent.

The ’559 patent describes a method of applying ultrasound energy to the dermis layer of the skin for the purpose of treating skin wrinkles and otherwise improving the appearance of the skin. *See, e.g.,* Ex. 1001 at Abstract, 1:57-2:12, 3:14-43. However, the methods claimed in the ’559 patent are not patentable. The claims would have been obvious over the prior art, including prior art that was never considered by the Patent Office but that was cited by the European Patent Office (“EPO”) as a novelty prior art reference in connection with a corresponding PCT application to the ’559 patent.

By way of background, the epidermis is the outermost layer of the skin. The dermis is located beneath the epidermis. A representative cross-section of human skin, which shows the epidermis and dermis, is reproduced below.



Ex. 1015 - The American Medical Association Encyclopedia of Medicine at p. 909

(*see also* Ex. 1003 ¶ 17)

It was known in the prior art that heating the dermis (also known as "hyperthermia") to a sufficient temperature caused skin to tighten. For example, it had been observed in burn patients that burns caused a tightening effect on the skin. Ex. 1005 at 1:24-25.

The mechanism by which heating the dermis caused skin to tighten was also understood in the prior art. The dermis primarily consists of collagen, which is an extracellular protein. *Id.* at 1:14; Ex. 1017 at p. 395. It was known that heating collagen within the dermis causes the collagen to denature and alters its physical

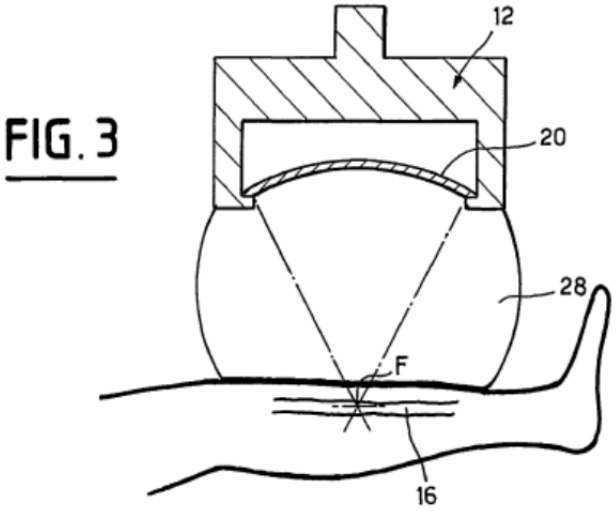
characteristics. Ex. 1005 at 1:16-18. Denaturing collagen stimulates a biological response that leads to the formation of new tissue within the dermis. *Id.* at 2:2-11.

Wrinkling of the skin is caused by inadequate support of the epidermis. *Id.* at 5:20-21. Replenishing the collagen matrix in the dermis, which provides the structural support for the epidermis, tightens the skin and corrects skin wrinkling. *Id.* at 5:20-26, 11:25-30.

Prior art International PCT Publication No. WO96/34568 to Knowlton ("Knowlton") describes the use of energy, including ultrasound, for treating wrinkles. *Id.* at 4:5-14, 6:25-27. Knowlton describes devices that are positioned on the outer surface of the skin and that apply energy through the skin to heat the dermis. *Id.* at Abstract, 8:27-9:5, 10:25-11:2. Knowlton explains that heating collagen in the skin induces a biological response that causes the skin to tighten and corrects wrinkling of the skin. *Id.* at 1:9-22, 5:20-26. Knowlton teaches that ultrasound is one suitable energy source for heating tissue. *Id.* at 11:3-7.

It was also well known in the prior art to use ultrasound to non-invasively treat tissue beneath the skin surface for purposes other than treating wrinkles. Prior art French Patent No. 2,672,486 to Technomed International (the "Technomed patent") describes the use of focused ultrasound for treating varicose skin structures, such as superficial varicose veins. Ex. 1007 at cover page, 2:15-

21, 5:1-10.[1] Figure 3 from the Technomed patent, which illustrates an ultrasound treatment device (12) focusing ultrasound energy at a focal region (F) of a varicose vein (16) beneath the skin surface is reproduced below.



Ex. 1007, Technomed Patent – Fig. 3

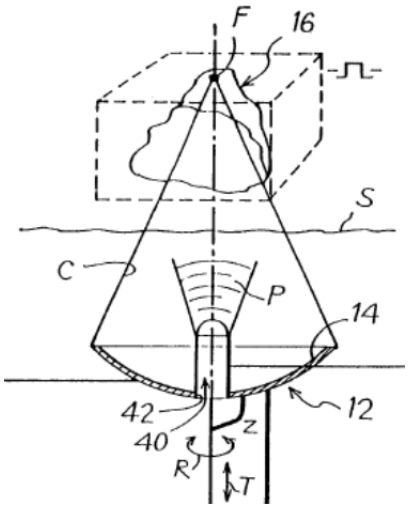
One skilled in the art would appreciate that varicose veins are located immediately beneath the skin and may be located within the dermis or may be located directly beneath and in contact with the dermis. Ex. 1003 ¶ 29; Ex. 1018 at

[1] Exhibit 1006 is a copy of the Technomed patent, which is written in French. Exhibit 1007 is an English translation of the patent. The citations in this Petition are to the English translation of the document. Exhibit 1012 is a declaration from the translator certifying the accuracy of the English translation (*see* ¶¶ 1-7).

p. 36. Consequently, treating superficial varicose veins as described in the Technomed patent is essentially treating tissue in the dermis. Ex. 1003 ¶ 29. The Technomed patent describes additional details on the structure and operation of focused ultrasound devices beyond what is taught in Knowlton, such as particular power levels that may be used. *Id.* ¶ 31; Ex. 1007 at 4:23-31.

Prior art International PCT Publication No. WO93/12742 to Technomed International ("Technomed PCT"), which shares some of the same named inventors as the Technomed patent, also describes treating tissue beneath the skin surface using focused ultrasound. Ex. 1009 at Abstract, 3:4-14.[2] An excerpt from Figure 1 of the patent that illustrates a treatment device (12) focusing ultrasound energy at a focal point (F) in tissue (16) located beneath the skin surface (S) is shown below.

[2] Technomed PCT was published in French. Exhibit 1008 is a copy of the published PCT application. Exhibit 1009 is an English translation of Technomed PCT. The citations in this Petition are to the English translation of the document. Exhibit 1012 is a declaration from the translator certifying the accuracy of the English translation (*see* ¶¶ 1-7). Exhibit 1010 is a copy of U.S. Patent No. 5,601,526, which claims priority to Technomed PCT.



Ex. 1009, Technomed PCT – Excerpt from Figure 1

Technomed PCT states that the disclosed methods are useful for a wide variety of treatments, including the treatment of skin tumors and of varicosities (*i.e.* varicose veins). *Id.* at 2:19-21, 8:1-5. Technomed PCT teaches that ultrasound can be used to heat tissue. *Id.* at Abstract, 1:3-5, 1:14-17. It also teaches that ultrasound can be used to cause cavitation, which results in the formation of bubbles in tissue that explode when they reach a critical size, thereby releasing energy into and treating the surrounding tissue. *Id.* at Abstract, 1:3-5, 1:18-21.

The ’559 patent describes and claims using focused ultrasound energy to heat the dermis and thereby cause a change in smoothness of the epidermis. Ex. 1001 at 8:26-29, claim 1. The patent theorizes that heating the dermis causes proteins in the dermis to denature and leads to the formation of new tissue that

causes a reduction in the appearance of wrinkles and otherwise improves the shape, smoothness and appearance of the skin. *Id.*

However, it was known in the prior art to use ultrasound to heat and treat tissue beneath the skin surface. As explained above, Knowlton describes using energy, including ultrasound, to heat and denature collagen for the purpose of tightening the skin and treating wrinkles. Ex. 1005 at Abstract, 1:9-22, 5:20-26, 8:27-9:5, 10:25-11:7. Knowlton describes heating the skin to temperatures within the same ranges disclosed in the '559 patent. *See, e.g., id.* at 16:9-15; Ex. 1001 at 8:40-46, Claim 1.

The Technomed patent provides further disclosure on using focused ultrasound to heat and treat tissue. Ex. 1007 at, *e.g.*, Abstract, 4:23-5:10. Notably, the Technomed patent was never considered by the U.S. Patent & Trademark Office ("PTO") during prosecution of the '559 patent. However, it was identified by the EPO as a novelty reference in connection with a corresponding PCT application claiming priority to the '559 patent. Ex. 1011 at pp. 46, 91, 119.[3] The EPO also subsequently cited the reasons provided in the PCT Preliminary

[3] Citations to file history page numbers are to the page numbers added by Petitioner at the bottom of the exhibit pages. Citations to other documents, such as patents and publications, are to the original page and line numbers of the documents.

Examination Report as a basis for objecting to the claims of the corresponding European application. *Id.* at p. 9.

Knowlton and the Technomed patent together teach all limitations of Claims 1-7 and 12-16 of the ’559 patent. Ex. 1003 ¶¶ 59-75. One skilled in the art would have been motivated to look to the Technomed patent, which contains a detailed disclosure regarding the use of focused ultrasound for heating tissue and also discloses safe and therapeutically effective power levels, and combine it with Knowlton. *Id.* ¶¶ 51-53. One skilled in the art would have been further motivated to combine the references because both describe focusing ultrasound energy to cause hyperthermia in tissue at the same or similar locations beneath the skin surface and describe treatments that improve the appearance of the skin. *Id.* ¶¶ 46-48

The ’559 patent also describes using focused ultrasound energy to cause a cavitation effect in the dermis. Ex. 1001 at 6:44-55. The patent theorizes that the cavitation effect “tears apart tissue in the dermis” and stimulates the formation of new tissue in the dermis. *Id.* at 8:62-9:3.

Knowlton and the Technomed patent do not explicitly disclose inducing cavitation in the dermis as required by dependent Claims 8-11 and as required by Claims 17-18 of the ’559 patent, which claim mechanically disrupting tissue.

However, Technomed PCT describes using ultrasound to treat tissue by creating both a thermal and cavitation effect. Ex. 1009 at Abstract, 1:3-5, 3:4-14.

One skilled in the art would have been motivated to combine Technomed PCT with Knowlton and the Technomed patent. Ex. 1003 ¶¶ 77-88. For example, each reference discloses the use of ultrasound for heating and treating tissue near the skin surface. *Id.* ¶ 78. Technomed PCT also teaches the benefits of using cavitation together with hyperthermia, which provides a further reason for combing it with Knowlton and the Technomed patent. *Id.* ¶ 84; Ex. 1009 at 8:12-15.

In sum, all claims of the '559 patent would have been obvious over the prior art. Ulthera now files the current Petition and requests that the Board institute an IPR on the grounds that: (1) Claims 1-7 and 12-16 are obvious over the combination of Knowlton and the Technomed patent, and (2) Claims 8-11 and 17-18 are obvious over the combination of Knowlton, the Technomed patent, and the Technomed PCT.

II. MANDATORY NOTICES UNDER 37 C.F.R. § 42.8(a)(1)

The following mandatory notices are provided as part of this Petition.

A. Real Party-In-Interest Under 37 C.F.R. § 42.8(b)(1)

The real parties-in-interest in this IPR are Ulthera, Inc.; Merz North America, Inc.; Merz Incorporated; Merz Pharmaceuticals GmbH; and Merz Pharma GmbH & Co. KGaA. These companies have corporate relationships with

many other companies, including the following members of the Merz family of companies: Merz GmbH & Co. KGaA; Merz Pharma GmbH; Friedrich Merz GmbH; Merz Holding GmbH & Co. KG; and Merz GmbH.

B. Related Matters Under 37 C.F.R. § 42.8(b)(2)

The '559 patent has been asserted by DermaFocus against Ulthera in *DermaFocus LLC v. Ulthera, Inc.*, No. 1:15-CV-00654-SLR (D. Del.), filed July 29, 2015.

C. Lead and Back-up Counsel Under 37 C.F.R. § 42.8(b)(3)

Petitioner provides the following designation of counsel.

Lead Counsel	**Backup Counsel**
Michelle E. Armond (Reg. No. 53,954) 2MEA@knobbe.com BoxUlthera@knobbe.com Postal and Hand-Delivery Address: Knobbe, Martens, Olson, & Bear, LLP 2040 Main St., 14th Fl. Irvine, CA 92614 Telephone: (949) 760-0404 Facsimile: (949) 760-9502	John B. Sganga, Jr. (Reg. No. 31,302) 2JBS@knobbe.com Matthew S. Bellinger (Reg. No. 46,547) 2MSB@knobbe.com Postal and Hand-Delivery Address: Knobbe, Martens, Olson, & Bear, LLP 2040 Main St., 14th Fl. Irvine, CA 92614 Telephone: (949) 760-0404 Facsimile: (949) 760-9502

Pursuant to 37 C.F.R. § 42.10(b), a Power of Attorney accompanies this Petition. The above identified Lead and Back-Up Counsel are registered practitioners associated with Customer No. 11-1410 listed in that Power of Attorney.

D. Service Information Under 37 C.F.R. § 42.8(b)(4)

Please address all correspondence to lead counsel and back-up counsel at the address shown above. Petitioner also consents to electronic service by email to: BoxUlthera@knobbe.com.

III. PAYMENT OF FEES PURSUANT TO 37 C.F.R. § 42.103

The $24,200 fee as required by 37 C.F.R. § 42.15(a) for this Petition has been paid. The undersigned authorizes payment for any additional fees that may be due in connection with this Petition to be charged to Deposit Account No. 11-1410.

IV. REQUIREMENTS FOR REVIEW UNDER 37 C.F.R. § 42.104

A. Grounds for Standing – 37 C.F.R. §42.104(a)

Ulthera hereby certifies that the ’559 patent is available for an IPR and that Ulthera is not barred or estopped from requesting an IPR on the grounds identified herein. Ulthera certifies that: (1) Ulthera is not the owner of the ’559 patent; (2) neither Ulthera, nor any real-party-in-interest, has filed a civil action challenging the validity of any claim of the ’559 patent; (3) neither Ulthera, nor any privy or real-party-in-interest, was served with a complaint alleging infringement of the ’559 patent more than one year prior to the filing of this Petition; (4) the estoppel provisions of 35 U.S.C. § 315(e)(1) do not prohibit this IPR; and (5) this Petition is being filed after the ’559 patent was granted.

B. Claims and Statutory Grounds – 37 C.F.R. § 42.104(b)(1) & (b)(2)

Ulthera requests institution of an IPR of Claims 1-18 of the ’559 patent in view of the following references, which are prior art for the following reasons:

- International PCT Publication No. WO96/34568 to Knowlton (Ex. 1005). Knowlton PCT was published on November 7, 1996. Ex. 1005 at cover page. Because Knowlton is a printed publication dated more than one year before the filing date of the ’559 patent, it is prior art under 35 U.S.C. § 102(b).
- French Patent No. 2,672,486 to Technomed International (Exs. 1006 and 1007). The Technomed patent was published on August 14, 1992. Ex. 1007 at cover page (identifying August 14, 1992 as the date the application was made available to the public). Because the Technomed patent is a printed publication dated more than one year before the filing date of the ’559 patent, it is prior art under 35 U.S.C. § 102(b).
- International PCT Publication No. WO93/12742 to Technomed International (Exs. 1008 and 1009). Technomed PCT was published on July 8, 1993. Ex. 1009 at cover page. Because Technomed PCT is a printed publication dated more than one year before the filing date of the ’559 patent, it is prior art under 35 U.S.C. § 102(b).

The proposed statutory grounds of rejection for the ’559 patent are as follows:

- Ground 1: Claims 1-7 and 12-16 are obvious over the combination of Knowlton and the Technomed patent.
- Ground 2: Claims 8-11 and 17-18 are obvious over the combination of Knowlton, the Technomed patent, and Technomed PCT.

C. Claim Construction – 37 C.F.R. § 42.104(b)(3)

Patent claim terms in an IPR are given their broadest reasonable interpretation in light of the specification to one having ordinary skill in the art. 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1275-79 (Fed. Cir. 2015) (“We conclude that Congress implicitly approved the broadest reasonable interpretation standard in enacting the AIA.”), *aff’d by Cuozzo Speed Techs., LLC v. Lee*, No. 15-446, __ U.S. ___ (June 20, 2016). Constructions under the broadest reasonable interpretation standard “cannot be divorced from the specification” and “must be consistent with the one that those skilled in the art would reach.” *Microsoft Corp. v. Proxyconn, Inc.*, 789 F.3d 1292, 1298 (Fed. Cir. 2015) (internal quotation marks and citations omitted).

Ulthera does not believe that the claims of the ’559 patent need to be expressly construed for purposes of this IPR proceeding in view of the prior art

relied upon in this Petition. The claims are invalid under any reasonable construction of the claim language.

Ulthera notes that the broadest reasonable construction standard applicable in an IPR is different from the claim construction standards applicable in district court litigation. Ulthera expressly reserves the right to advocate different claim constructions under the applicable standards in other proceedings involving the '559 patent, including the co-pending district court action. However, whether the claims are viewed under a broadest reasonable interpretation standard or under the claim construction standard applicable in district court, the claims are invalid for the reasons identified in this Petition.

D. Unpatentability of Construed Claims – 37 C.F.R. § 42.104(b)(4)

A detailed explanation of how the claims of the '559 patent are unpatentable, including an identification of where each claim limitation is found in the prior art, is provided in Section V below.

E. Supporting Evidence – 37 C.F.R. § 42.104(b)(5)

The exhibit numbers of the supporting evidence relied upon to support the challenge, and the relevance of the evidence to the challenge, including specific portions of the evidence relied on to support the challenge, are provided in Section V below. An Exhibit List with exhibit numbers and a brief description of each exhibit is included herewith.

Ulthera also submits the declaration of technical expert Mark Schafer, Ph.D. in support of this Petition in accordance with 37 C.F.R. § 1.68. Ex. 1003. Dr. Schafer has extensive industry experience with ultrasound technology for use in clinical applications. *Id*. ¶¶ 3-8; Ex. 1004. Dr. Schafer's declaration explains the basis for his conclusions that the claims of the '559 patent would have been obvious.

Ulthera also submits the declaration of John Speese III in support of this Petition in accordance with 37 C.F.R. § 1.68. Ex. 1012. The declaration certifies the accuracy of the English translations of the Technomed Patent and Technomed PCT references filed with this Petition. Exs. 1007, 1009.

V. THE CLAIMS OF THE '559 PATENT ARE OBVIOUS

Claims 1-18 of the '559 patent are unpatentable as obvious. Claims 1-7 and 12-16 would have been obvious over the combination of Knowlton and the Technomed patent. Ex. 1003 ¶¶ 14, 45-75. Claims 8-11 and 17-18 would have been obvious over the combination of Knowlton, the Technomed patent, and Technomed PCT. *Id.* ¶¶ 15, 76-97.

A. Legal Standard for Obviousness

A claim is obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill

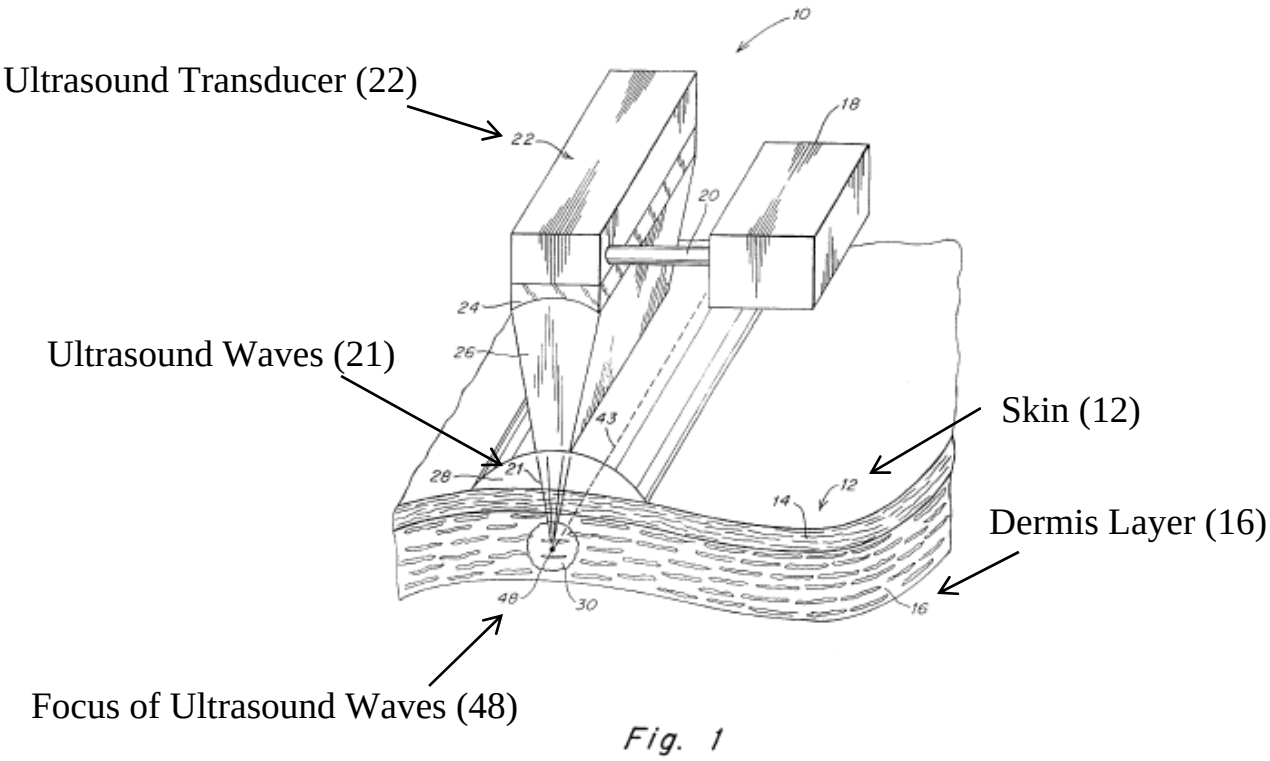
in the art to which said subject matter pertains." 35 U.S.C. § 103. The obviousness analysis includes an assessment of the *Graham* factors: (1) the scope and content of the prior art; (2) any differences between the claims and the prior art; (3) the level of ordinary skill in the art; and (4) where in evidence, objective indicia of non-obviousness. *KSR Int'l Co., v. Teleflex Inc*., 550 U.S. 398, 406 (2007) (citing *Graham v. John Deere Co*., 383 U.S. 1, 17-18 (1966)).

Some limitations of the '559 patent recite ranges, such as ranges of temperatures or power levels. Ex. 1001 at Claims 1 and 6. "Where a claimed range overlaps with a range disclosed in the prior art, there is a presumption of obviousness." *Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1311 (Fed. Cir. 2006). "[E]ven a slight overlap in range establishes a *prima facie* case of obviousness." *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003). When "the claimed ranges are completely encompassed by the prior art, the conclusion is even more compelling than in cases of mere overlap." *Id.* at 1330; *Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 736–41 (Fed. Cir. 2013) (finding claims obvious where prior art disclosing concentrations of 0.01%–1% adapalene encompassed the claimed concentration of 0.3% adapalene). The presumption of obviousness can be rebutted if it can be shown that the prior art teaches away from the claimed range, the claimed range produces new and unexpected results, or

there are other pertinent secondary considerations of non-obviousness. *Ormco*, 463 F.3d at 1311; *Galderma Labs.*, 737 F.3d at 738.

B. The Purported Invention of the ’559 Patent

The ’559 patent describes a system for skin rejuvenation, including reducing skin wrinkles, using focused ultrasound energy. Ex. 1001 at Abstract, 1:57-2:4. The patent describes focusing ultrasound energy in the dermis layer of the skin to heat the dermis and/or to induce cavitation in the dermis. *Id.* at 3:27-37, 8:40-9:3. Figure 1 from the patent (with text labels added), which illustrates an ultrasound transducer device focusing ultrasound energy in the dermis layer, is shown below.



Ex. 1001, ’559 Patent – Fig. 1 (text labels added)

The patent alleges that heating or inducing cavitation in the dermis by applying focused ultrasound energy "stimulates" or "irritates" the dermis. *Id.* at 2:13-23, 3:14-22. The patent further speculates that while "the biological mechanism is not completely understood, it appears that hyperthermia and/or cavitation either alone or in combination, appear to cause a biological response" that reduces the appearance of skin wrinkles. *Id.* at 8:27-39.

With respect to hyperthermia, the patent teaches using ultrasound energy to heat the dermis to a temperature between 47º and 75º Celsius. *Id.* at 8:40-46. The patent states that heating the dermis within that temperature range causes proteins within the dermis to denature and leads to the formation of new tissue in the dermis. *Id.* at 8:30-46.

The '559 patent describes the cavitation process as using ultrasound energy to form bubbles or cavities in the dermis. *Id.* at 8:62-66. The patent states that when the cavitational bubbles collapse, "a shock wave results that mechanically, in as localized area, tears apart tissue in the dermis causing dermal inflammation and a resultant biological response." *Id.* at 8:66-9:2.

The '559 patent acknowledges that the use of ultrasound for treating tissue was known in the prior art. The '559 patent concedes that the focused ultrasound device shown in Figure 1 of the patent is similar to a device described in prior art

U.S. Patent No. 5,230,334 ("the '334 patent") to the same named inventor, Peter Klopotek. Ex. 1001 at 3:44-4:2; Ex. 1013 ('334 patent).

The '559 patent characterizes the prior art '334 patent as describing a method and apparatus for generating localized hyperthermia in human tissue, particularly in the collagen fibers of the cornea. Ex. 1001 at 3:46-48. The '559 patent distinguishes the '334 patent by asserting that the methods described in the '334 patent use higher power levels than the methods described in the '559 patent. *Id.* at 3:51-4:2. The '559 patent describes power levels ranging from 500 to 1500 watts/cm^2 at the focal point in the dermis layer. *Id.* at 9:10-13.

During prosecution of the '559 patent, in response to a double patenting rejection issued by the PTO over the claims of the '334 patent, the applicant similarly argued that it would not have been obvious to adjust the power levels of the device described in the '334 patent to utilize power levels that would treat wrinkles but not cause damage to the skin. Ex. 1002 at p. 72. The applicant made a similar argument in responding to an obviousness rejection made by the PTO in view of the '334 patent. *Id.* at p. 78.

However, it was known in the prior art to use focused ultrasound within the power level ranges described in the '559 patent for treating tissue beneath the skin surface. The Technomed patent describes focused ultrasound using power levels within the range claimed by the '559 patent. *See*, *e.g.*, Ex. 1007 at 2:15-21

(describing "means of transmitting ultrasonic waves capable of producing in said focal region an ultrasonic intensity of between about 100 W/cm^2 and about 2 kW/cm^2, and preferably between 100 W/cm^2 and 500 W/cm^2"); Ex. 1001 at Claim 6 ("The method of Claim 3, wherein a step of depositing energy further comprises using power levels in the range of approximately 500 W/cm^2 to 1500 W/cm^2 at the focal point of the ultrasound beam.").

C. Prosecution History Summary

The '559 patent issued from U.S. Application No. 08/998,963, filed on December 29, 1997. A copy of the file history is submitted as Exhibit 1002.

At no time during prosecution of the '559 patent did the Examiner consider the Technomed patent or Technomed PCT. The Examiner also did not consider the Knowlton PCT reference.

U.S. Patent No. 5,755,753 to Knowlton ("the Knowlton '753 patent"), which is one of the applications to which Knowlton PCT claims priority, was referenced by the Examiner during prosecution of the '559 patent in connection with a double patenting rejection and in discussing reasons to combine cited references. Ex. 1002 at pp. 89-90, 180-181. However, the Examiner did not cite the Knowlton '753 patent when rejecting the pending claims as obvious over the prior art. *Id.* at pp. 92-94, 183-185. Moreover, the Knowlton '753 patent was only potentially prior art under 35 U.S.C. § 102(a) given its filing date and issue date. Ex. 1014. In

contrast, the Knowlton PCT reference, which was not considered by the Examiner, is prior art under 35 U.S.C. § 102(b) because it was published on November 7, 1996. Ex. 1005 at cover page.

D. Level of Ordinary Skill in the Art

A person having ordinary skill in the field of the subject matter described in the ’559 patent would have at least a bachelor’s degree in electrical, mechanical, or biomedical engineering with at least 4-5 years of work experience designing and/or working with medical devices using energy for the treatment of tissue, with at least some experience with focused ultrasound, and would be familiar with the anatomy/biology of the areas that the medical devices are intended to treat, or a master’s degree in electrical, mechanical, or biomedical engineering with at least 2-3 years of work experience and other knowledge as discussed above. Ex. 1003 ¶¶ 42-44.

E. Overview of the Prior Art

The prior art references – Knowlton, the Technomed patent, and Technomed PCT – that form the basis for Petitioner’s statutory grounds for invalidity are summarized below.

1. Knowlton

Knowlton describes a skin resurfacing device and process that delivers energy through the skin to heat collagen beneath the skin surface, including in the

dermis. Ex. 1005 at Abstract, 1:14-18; 8:29-9:4; Ex. 1003 ¶¶ 24-25. Knowlton explains that the process can be used for various applications, including tightening the skin and treating wrinkles. Ex. 1005 at Abstract, 5:13-19 ("Suitable applications for the methods of the present invention include but are not limited to, … laxity and wrinkling of the skin…."), 5:20-29, 9:28-10:2.

Knowlton also recognized and explained the relationship between denaturing proteins in the dermis and reducing the appearance of wrinkles. Knowlton teaches in one embodiment heating collagen in the deeper dermis to above 65º Celsius in order to denature and shrink the collagen, and also describes heating surface tissue to a temperature between 40º and 60º Celsius and underlying collagen to a temperature between 60º and 80º Celsius in order to obtain the desired outcome of tightening the skin and treating wrinkles. *Id.* at 6:3-4, 16:10-13, *see also* p. 26, Claim 49 ("wherein the underlying tissue site is heated to a temperature of 40 to 80 degrees or greater"). Knowlton also states that in some embodiments the temperature ranges can be broader. *Id.* at 16:13-15. The temperatures disclosed in Knowlton overlap with and encompass the range described and claimed in the '559 patent of heating tissue in the dermis to a temperature between 47º and 75º Celsius. Ex. 1001 at 8:40-61, Claim 1.

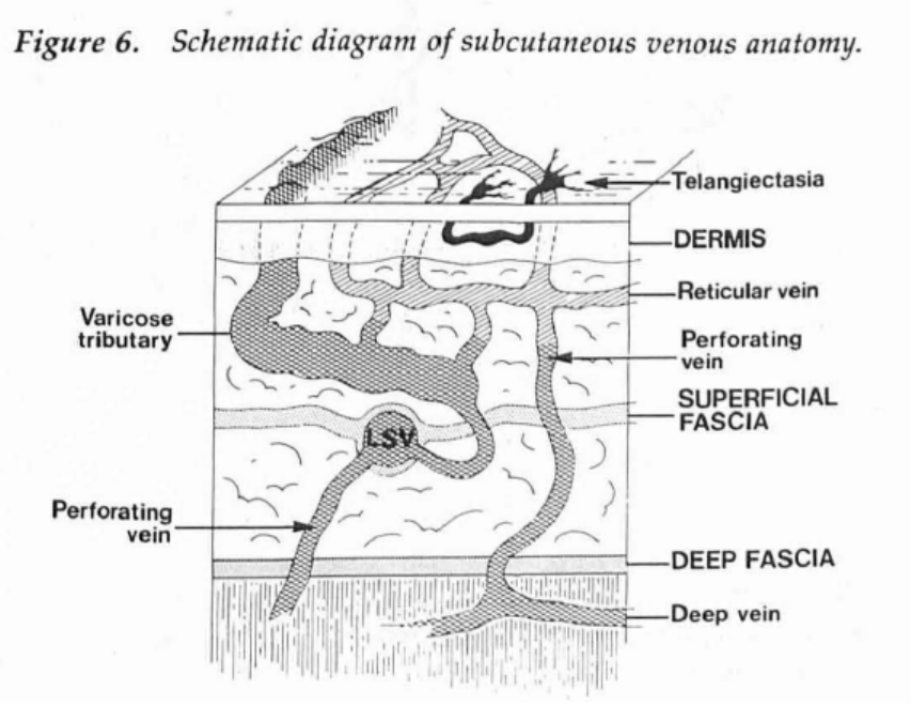
Knowlton teaches that ultrasound is one of the energy sources that can be used to heat the dermis. Ex. 1005 at 6:25-27, 11:3-7. Knowlton provides a

description of how focused ultrasound is used to treat collagen tissue beneath the skin surface. *Id.* at 14:29-15:8. Knowlton also cites two secondary references that provide further information on the use of focused ultrasound. *Id.* at 15:1-8, citing *Ultrasonics Theory and Application* (Ex. 1019) and *Deep Local Hypothermia [sic – Hyperthermia] for Cancer Therapy: Extreme [sic – External] Electromagnetic and Ultrasound Technics [sic – Techniques]* (Ex. 1020).

Knowlton explains that reducing wrinkles is achieved while minimizing damage to the skin surface. Ex. 1005 at 1:9-11, 3:16-18, 5:20-29, 10:3-13. Similar to the ’559 patent, Knowlton also describes performing multiple treatments over a course of time to achieve the desired result. *Id.* at 6:5-6, 10:31-11:1, 16:2-5.

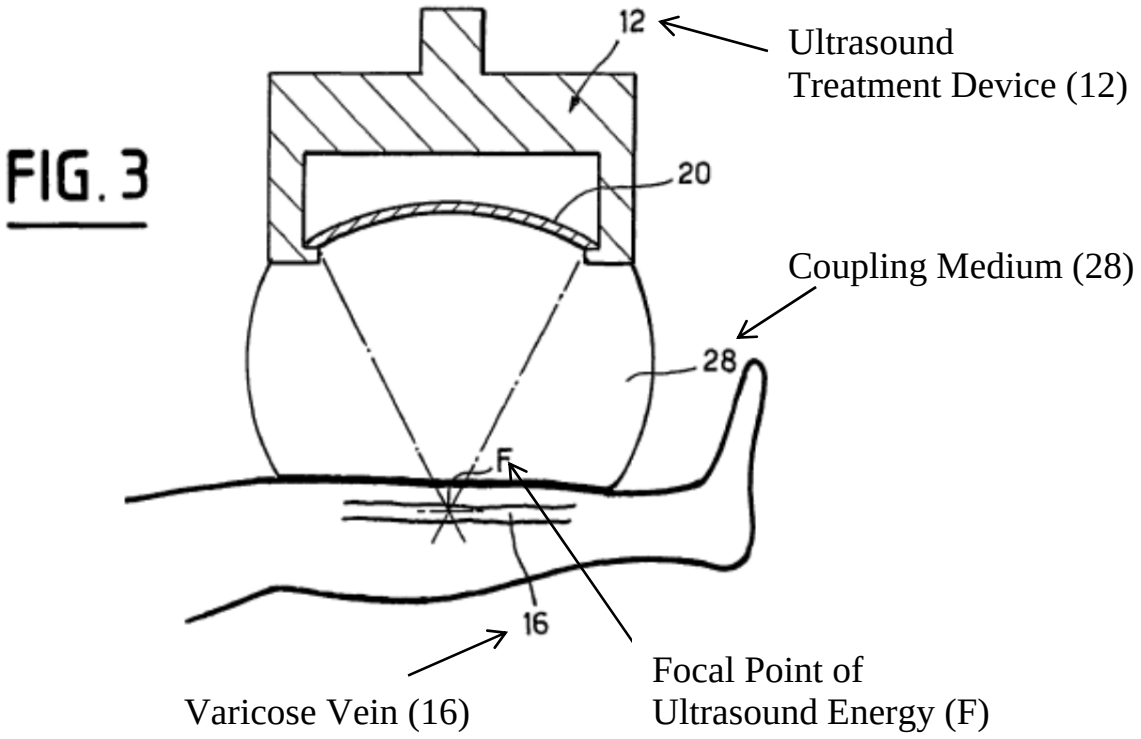
2. <u>The Technomed Patent</u>

The Technomed patent describes the use of focused ultrasound for a variety of therapeutic uses, including treating superficial varicose veins. Ex. 1007 at 1:3-4, 2:15-21, 13:9-11; Ex. 1003 ¶¶ 26-28. One skilled in the art would understand that various blood vessels and capillaries are located within the dermis. Ex. 1003 ¶ 29; Ex. 1015 at pp. 909-910; Ex. 1018 at p. 39. A person skilled in the art would also appreciate that varicose veins are located immediately beneath the skin and may be located within the dermis or directly beneath and in contact with the dermis. Ex. 1003 ¶ 29; Ex. 1018 at p. 36. An exemplary image showing venous anatomy, including veins extending through the dermis, is shown below.



Ex. 1018 - Anatomy of the Superficial Venous System, *Dermatol. Surg.* (1995) at p. 39

The Technomed patent describes using focused ultrasound to heat the area beneath the skin that is being treated. Ex. 1007 at 2:1-4, 5:1-10. Figure 3 of the Technomed patent (with text labels added), shown below, illustrates one exemplary embodiment described in the patent. *See also id.* at 7:25-8:13.



Ex. 1007, Technomed Patent – Fig. 3 (text labels added)

The Technomed patent teaches heating varicose veins to cause the thermal destruction of the veins. *Id.* at 5:1-10. The Technomed patent discloses a variety of treatment parameters, such as power, frequency and treatment times. *Id.* at 4:23-5:16. The patent describes the use of power levels ranging from 100 watts/cm^2 to 2 kilowatts/cm^2 at the focal region of the tissue being treated, which subsumes the power levels disclosed and claimed in the ’559 patent. *Id.* at 2:15-21, 4:28-31, 11:30-12:5.

The Technomed patent was not disclosed to or considered by the PTO during prosecution of the ’559 patent, even though it had been identified as an “X”

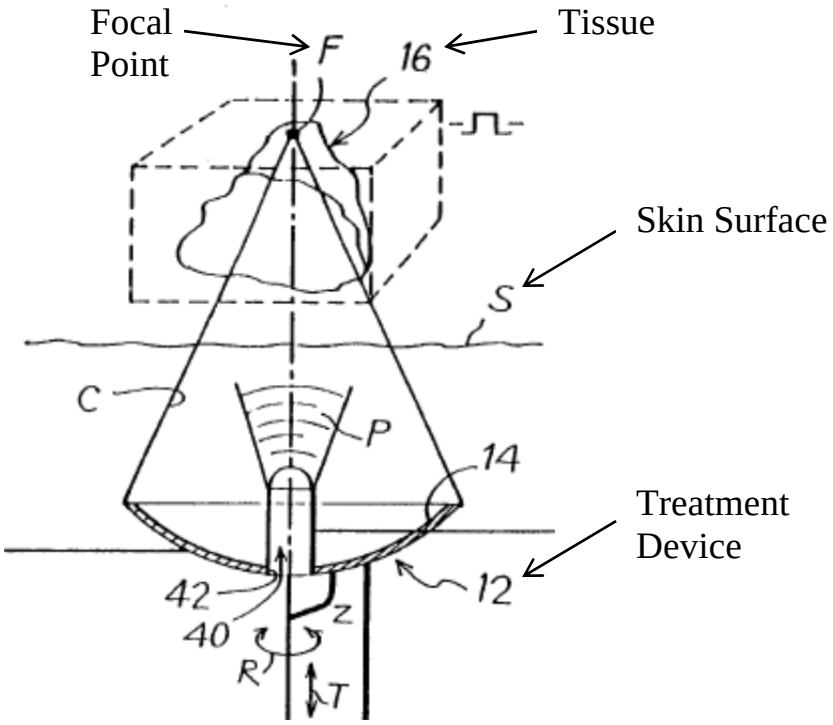
or novelty reference in a search report for a corresponding PCT application claiming priority to the ’559 patent. Ex. 1011 at p. 119. The Technomed patent was also cited as a novelty reference in a subsequent PCT Written Opinion and PCT Preliminary Examination Report issued by the EPO. *Id.* at pp. 46 and 61. The same counsel represented the ’559 patent applicant in connection with the U.S. prosecution and the PCT proceedings. Ex. 1002 at pp. 170-171; Ex. 1011 at p. 58. During prosecution of the corresponding European application, the EPO also cited the reasons provided in the PCT Preliminary Examination Report as a basis for objecting to the claims. Ex. 1011 at p. 9. The applicant thereafter abandoned the European application. *Id.* at p. 1. The fact that the Technomed patent was not cited during the prosecution of the ’559 patent denied the public of the interest that Congress intended to protect with 37 C.F.R. § 1.56.

3. Technomed PCT

Technomed PCT names two of the same inventors as the Technomed patent. Ex. 1009. Like the Technomed patent, Technomed PCT was not considered by the PTO during prosecution of the ’559 patent.

Technomed PCT describes the use of focused ultrasound for treating tissue located beneath the skin surface. *Id.* at Abstract, 1:3-5, 3:4-14, 10:4-15; Ex. 1003 ¶¶ 32-33. Technomed PCT teaches that the disclosed ultrasound therapy devices have a range of uses, including treatment of varicosities (*i.e.* varicose veins) and

skin tumors, among others. Ex. 1009 at 8:1-7; Ex. 1003 ¶ 36. An excerpt from Figure 1 of Technomed PCT, which depicts focusing ultrasound at a particular location to treat tissue beneath the skin surface, is reproduced below.



Ex. 1009, Technomed PCT – Excerpt of Fig. 1 (text labels added)

Technomed PCT describes using ultrasound for causing hyperthermia and/or cavitation in tissue, and teaches that tissue may be treated using both hyperthermia and cavitation in combination. Ex. 1009 at 1:3-5, 3:4-14; Ex. 1003 ¶¶ 34-36. It explains that a benefit of combining hyperthermia with cavitation is that the destructive nature of the treatment is reinforced, which consequently limits the duration of the treatment pulses and thus avoids the undesirable spread of heat energy within the tissue. Ex. 1009 at 8:12-15. Technomed PCT discloses different

frequencies, power levels, and other variables that can be used depending upon the desired result to be obtained. *Id.* at 4:6-19, 5:9-17, 14:2-4.

F. Ground 1: Obviousness of Claims 1-7 and 12-16 Over Knowlton in View of the Technomed Patent

Claim 1 of the '559 patent, the only independent claim, claims a method for rejuvenating human skin. Claim 1, and dependent Claims 6-7 and 12-16, would have been obvious over Knowlton in view of the Technomed patent.

1. Reasons to Combine Knowlton and the Technomed Patent

It would have been obvious for one skilled in the art to combine Knowlton and the Technomed patent. Ex. 1003 ¶¶ 46-56. Both references are directed to the same technical subject matter, namely systems for passing energy through the skin to heat and treat tissue located under the skin surface and that result in an improved appearance of the skin. *Id.* ¶¶ 24-25, 27-28, 30, 46-48, 55. Both references also identify ultrasound as an energy source. *Id.* ¶¶ 25, 26-27, 47. Because the methods described in Knowlton and the Technomed patent are so similar, one skilled in the art would appreciate that the focused ultrasound system described in the Technomed patent is compatible with the disclosure of Knowlton, and would have been motivated to combine the teachings of the two references. *Id.* ¶ 49.

While Knowlton teaches that ultrasound is one energy source that may be used for tightening the skin and treating wrinkles (Ex. 1005 at 11:3-7), and provides a description of using focused ultrasound (*id.* at 14:29-15:8), Knowlton

does not explicitly disclose specific ultrasound frequencies or power levels. One skilled in the art seeking to use ultrasound as described in Knowlton to treat the skin would understand that a set number of routine, operational parameters would need to be selected, such as power levels. Ex. 1003 ¶¶ 53, 56. One skilled in the art would have been motivated to look at the Technomed patent, which identifies ultrasound power levels that are safe and clinically effective for treating tissue beneath the skin surface. *Id.* ¶ 51.

The Technomed patent also provides additional details on the structure and operation of a focused ultrasound system that are not included in Knowlton. *Id.* ¶ 52. Accordingly, one skilled in the art would have been further motivated to look to the more detailed disclosure of focused ultrasound in the Technomed patent and combine it with the more general teaching in Knowlton of using ultrasound for tightening skin and treating wrinkles. *Id.* ¶ 53.

Knowlton and the Technomed patent also both describe treating tissue located in the same or similar locations beneath the skin surface. *Id.* ¶ 48. Knowlton describes focusing energy in the dermis, while the Technomed patent describes treatment of superficial varicose veins, which one skilled in the art would understand may be located within the dermis or directly beneath and in contact with the dermis. *Id.* ¶ 29. One skilled in the art would appreciate that the treatment of superficial varicose veins described in the Technomed patent, which

describes a treatment zone or focal region where ultrasound waves are focused (Ex. 1007 at 5:3-4, 5:20-23, 12:4-5), would result in ultrasound energy being focused in the dermis due to reasons such as limitations in imaging and focusing on the target area, the irregular shape of the veins, and patient movement. Ex. 1003 ¶ 54. Consequently, one skilled in the art would have appreciated that the methods described in the Technomed patent would be safe for use in the dermis and would have recognized the applicability of the disclosed methods to the methods disclosed in Knowlton. Ex. 1003 ¶¶ 50, 54.

Also, persons working in the field of energy based therapeutic devices would have appreciated that a particular device may have a variety of potential uses or applications. *Id.* ¶ 49. One skilled in the art would have recognized that the devices and methods disclosed in the Technomed patent were not necessarily limited to only treating varicose veins and would have other suitable uses, particularly with respect to the treatment of similarly located tissue, such as the dermis. *Id.* Notably, treating superficial varicose veins is much closer to treating the dermis than the disclosure in the prior art ’334 patent to Klopotek of treating the cornea, which the PTO used as a basis for rejecting the ’559 patent claims during prosecution. Ex. 1002 at pp. 57-59, 91-95.

In addition, Knowlton and the Technomed patent describe similar mechanisms of applying heat to tissue to cause an irreversible change in tissue

structure that leads to the desired treatment result. Ex. 1003 ¶ 55. Moreover, varicose veins often arise from laxity of the vein walls that causes wrinkling of the veins and manifest themselves as wrinkled structures visible through the skin surface. *Id.* Knowlton addresses a similar problem of tightening skin and treating wrinkles. For these additional reasons, one skilled the art would have been motivated to combine the Technomed patent with Knowlton. *Id.*

2. Differences Between the Prior Art and Claims 1-7 and 12-16 of the '559 Patent

Knowlton discloses nearly all limitations of Claims 1-7 and 12-16. Dependent Claim 6 requires that the step of depositing energy in the dermis layer further comprises a power level in the range of approximately 500 watts/cm^2 to 1500 watts/cm^2 at the focal point of the ultrasound beam. Knowlton does not identify specific numerical ultrasound power levels. Ex. 1003 ¶ 58. However, the Technomed patent discloses power levels in the range of 100 watts/cm^2 and 2 kilowatts/cm^2 at the focal region of tissue being treated. Ex. 1007 at 2:15-21; Ex. 1003 ¶ 31.

While the Technomed patent discloses the use of focused ultrasound, it does not explicitly disclose "depositing energy in the dermis layer sufficient to heat tissue within the layer to a temperature ranging from about 47º C. to about 75º C. to stimulate or irritate a dermis layer" as required by Claim 1. But the Technomed patent's teaching that the described device may be used for treating superficial

varicose veins would convey to one skilled in the art that energy would be deposited in or near the dermis, causing heating of the dermis. Ex. 1007 at cover, 1:3-4; Ex. 1003 ¶ 54. Moreover, Knowlton expressly discloses the claimed limitations regarding the temperature to be reached in the dermis. Ex. 1005 at 6:3-4, 16:9-15; Ex. 1003 ¶ 63.

3. Claim Charts

The following sections contain specific citations to the disclosures of Knowlton and the Technomed patent that disclose all of the limitations of Claims 1-7 and 12-16 of the '559 patent. More detailed claim charts are included in the accompanying declaration of Dr. Schafer. Ex. 1003 ¶¶ 59-75.

a. Claim 1

Knowlton and the Technomed patent together teach each limitation of Claim 1. To the extent the preamble of Claim 1 is considered to be a claim limitation, Knowlton and the Technomed patent both disclose "a method of rejuvenating human skin." Ex. 1003 ¶ 60. Knowlton describes that the disclosed processes may be used for tightening the skin and treating wrinkles, which both improve or rejuvenate the appearance of the skin. Ex. 1005 at 3:16-18, 5:13-19, 9:28-10:2. The Technomed patent states that the disclosed processes may be used for treating superficial varicose veins. Ex. 1007 at Abstract, 1:3-4. Eliminating or reducing

the appearance of superficial varicose veins also rejuvenates or improves the appearance of the skin. Ex. 1003 ¶¶ 30, 60.

Knowlton and the Technomed patent both disclose "identifying a region of the skin to be treated." *Id.* ¶ 61. Knowlton discloses identifying areas for tightening or treating wrinkles, and identifies specific body areas that may be treated. Ex. 1005 at 2:12-13, 3:16-18, 5:20-29, 14:8-11. The Technomed patent describes identifying for treatment skin areas containing underlying varicose veins. Ex. 1007 at cover, 1:3-4, 3:21-29, 13:9-11.

Knowlton also discloses "focusing ultrasound energy in a dermis layer of the region of skin." Ex. 1003 ¶ 62. Knowlton teaches that the dermis is composed primarily of collagen and that the dermis provides the main structural support for the skin. Ex. 1005 at 1:9-14. Knowlton further teaches that wrinkling of the skin occurs as a consequence of inadequate support of epidermis. *Id.* at 5:20-21. Knowlton describes using energy to heat and denature collagen beneath the skin surface, including in the dermis layer. *Id.* at 11:25-27. Knowlton also describes that ultrasound is one of the energy sources that can be used and describes the use of focused ultrasound. *Id.* at 11:3-7, 15:1-8.

The Technomed patent describes applying focused ultrasound to treat superficial varicose veins. Ex. 1007 at 2:15-21. One skilled in the art would recognize that varicose veins may be located within the dermis. Ex. 1003 ¶ 29; Ex.

1018 at pp. 36, 39. For the reasons discussed above, one skilled in the art would also appreciate that the focused ultrasound described in the Technomed patent could not be focused at all times precisely on the vein being treated, and that the focused ultrasound may also be applied to tissue surrounding the vein, including the dermis. Ex. 1003 ¶ 54.

Knowlton also discloses "depositing energy in the dermis layer sufficient to heat tissue within the layer to a temperature ranging from about 47º C. to about 75º C." Ex. 1003 ¶ 63. For example, Knowlton states: "In one embodiment the deeper dermis is heated to above 65 degrees for collagen contraction." Ex. 1005 at 6:3-4. Knowlton further describes heating skin to temperature ranges from about 40º C to 80º C. *Id.* at 16:9-13, *see also id.* at Claim 49 ("… wherein the underlying tissue site is heated to a temperature of 40 to 80 degrees or greater.").

The temperatures disclosed in Knowlton fall within and encompass the temperature range of Claim 1 of the '559 patent and renders the claimed temperature range obvious. *See Ormco*, 463 F.3d at 1310–11 (finding claimed range of 2–20 days for replacing dental appliances would have been obvious in view of prior teaching that appliances should be replaced every 14 to 21 days); *In re Peterson*, 315 F.3d at 1330. Further, in view of the disclosure in Knowlton of temperature ranges for heating collagen that closely track the ranges set forth in

Claim 1 of the ’559 patent, one skilled in the art would have found the claimed range of 47º C to about 75º C obvious. Ex. 1003 ¶ 63.

The Technomed patent similarly describes using focused ultrasound to heat and treat varicose veins. Ex. 1007 at 5:6-10. Given the positioning varicose veins in relation to the dermis, one skilled in the art would understand that applying focused ultrasound as described in the Technomed patent would also heat the dermis. Ex. 1003 ¶ 54.

The Technomed patent does not describe specific temperatures at the treatment site obtained through use of the disclosed inventions. However, in describing a prior art technique for using focused ultrasound to treat varicose veins, the Technomed patent states: “Temperatures obtained at 2 mm from the focal point are about 55º C for an exposure of 5 seconds.” Ex. 1007 at 1:21-22. The temperature of 55º C is within the range claimed by Claim 1 of the ’559 patent.

Knowlton also describes heating the dermis “to stimulate or irritate a dermis layer in the region of the skin.” Ex. 1003 ¶ 64. Knowlton describes heating the dermis using the same temperatures disclosed and claimed in the ’559 patent. Ex. 1005 at 4:11-14, 16:9-13. Knowlton also discloses the same biological mechanism for tightening the skin or treating wrinkles, namely heating the tissue to denature collagen, described in the ’559 patent. *See, e.g., id.* at 1:9-2:11, 5:20-26; Ex. 1001 at 8:26-39.

Knowlton further discloses stimulating or irritating the dermis "so as to cause a change in the dermis layer of the skin that results in a change in a smoothness of an epidermis layer of the skin." Ex. 1003 ¶ 64. For example, Knowlton explains that heating collagen causes a biological response that causes the skin to tighten. Ex. 1005 at 11:25-30. Knowlton also states that the disclosed methods can be used for treating skin wrinkling. *Id.* at 5:13-26. Reducing or eliminating wrinkles constitutes a change in a smoothness of an epidermis layer of the skin. Ex. 1003 ¶ 64.

The Technomed patent describes a treatment for eliminating varicose veins, including superficial varicose veins. Ex. 1007 at Abstract, 1:3-4. The treatment of varicose veins eliminates or reduces the appearance of bulging veins and results in a smoothing of the skin surface and an improvement in the appearance of the skin. Ex. 1003 ¶ 64.

The following claim chart contains additional information regarding how Knowlton and the Technomed patent disclose each element of Claim 1 of the '559 patent.

Claim 1	Knowlton/Technomed Patent
1. A method of rejuvenating human skin, the method comprising	Knowlton discloses methods for rejuvenating human skin through tightening of skin and treatment of wrinkles. Knowlton, which is titled "Apparatus For Skin Resurfacing," discloses: "[a]n object of the present invention to provide [sic] a method and apparatus for ***tightening skin*** without substantially damaging the melanocytes and other epithelial cells." Ex. 1005 at 3:16-

Claim 1	Knowlton/Technomed Patent
	18 (emphases added); *see also* 5:13-19 ("***Suitable applications for the methods of the present invention include*** but are not limited to … ***wrinkling of the skin***….") (emphases added); Ex. 1003 ¶ 60. The Technomed patent describes methods for treating skin using focused ultrasound, including treatment of superficial varicose veins: "The present invention essentially concerns an ultrasound apparatus for the extracorporeal therapeutic treatment of varicosities and superficial varicose veins." Ex. 1007 at 1:3-4. The treatment of varicose veins results in an improved appearance of the skin. Ex. 1003 ¶¶ 30, 60.
identifying a region of skin to be treated;	Knowlton identifies particular areas of the skin for treatment: "Skin tightening with a reverse thermal gradient contraction of collagen can correct areas including but not limited to the thighs, knees, arms, back and hips without unsightly scarring of standard techniques." Ex. 1005 at 14:8-11; *see also* 2:12-13 and 3:16-18 (discussing tightening the skin); Ex. 1003 ¶ 61. The Technomed patent also teaches identifying a region of skin to be treated. The Technomed patent describes: "According to yet another particularly useful embodiment of the invention, means are provided for marking on the surface of the zone of the skin to be treated, for example a marker pen, a felt pen or a fluorescent marker." Ex. 1007 at 3:18-20. The Technomed patent describes identifying and treating superficial varicose veins, which are located immediately beneath the skin surface. *Id.* at cover, 1:3-4, 13:9-11, *see also* 3:30-4:10 and 5:20-23 (describing the identification of the area to be treated); Ex. 1003 ¶ 61.
focusing ultrasound energy in a dermis layer of the region of skin; and	Knowlton teaches: "[i]n one method of the present invention, ***collagen tissue in a dermis*** underlying the epidermis of the skin is transcutaneously contracted with the use of a thermal heating apparatus." Ex. 1005 at 11:25-27 (emphases added), *see also* 1:9-14, 5:20-26; Ex.

Claim 1	Knowlton/Technomed Patent
	1003 ¶ 62. Knowlton explains that various energy sources, including ultrasound, can be used for heating collagen: "Various types of electromagnetic energy can be utilized with the present invention. Electromagnetic energy may be any kind that can cause cell heating or physical destruction by being applied to collagen tissue. ***Examples of suitable electromagnetic energy sources include***, but are not limited to RF, microwave, ***ultrasound***, laser and the like." Ex. 1005 at 11:3-7 (emphases added), 6:25-26, *see also* 15:1-8 (providing details on structure and use of focused ultrasound device); Ex. 1003 ¶ 62. The Technomed patent describes using focused ultrasound to heat and treat varicose veins. Ex. 1007 at 5:6-10 ("The ultrasonic wave transmission means is made to transmit ultrasonic waves that are focused by the ultrasonic treatment device in said focal region with an ultrasonic intensity in the focal region of between 100 W/cm^2 and 2 kW/cm^2 for a sufficient period of time to accomplish the thermal destruction of the endothelium of the veins, leading in a few days to the thrombosis of said vein."), 2:17-21, 5:1-10, Figs. 3-4; Ex. 1003 ¶ 62. One skilled in the art would also appreciate that use of the methods described in the Technomed patent would result in focused ultrasound being applied to tissue surrounding the vein, including the dermis. Ex. 1003 ¶¶ 29, 54, 62.
depositing energy in the dermis layer sufficient to heat tissue within the layer to a temperature ranging from about 47º C. to about 75º C.	Knowlton states: "[i]n one method of the present invention, ***collagen tissue in a dermis*** underlying the epidermis of the skin is transcutaneously contracted with the ***use of a thermal heating apparatus***." Ex. 1005 at 11:25-27 (emphases added), *see also* 1:9-14, 5:20-6:7 (describing collagen located in dermis layer and describing heating and denaturing collagen); Ex. 1003 ¶ 63. Knowlton states: "[t]he reverse thermal gradient provides a variation in temperature throughout the various tissue

Claim 1	Knowlton/Technomed Patent
	layers. For example, in various embodiments, the reverse thermal gradient has a tissue surface temperature range from about ***40 to 60 degrees C***, and a selected underlying tissue site temperature, i.e., where scar collagen is formed or where collagen is contracted, of about ***60 to 80 degrees C***." Ex. 1005 at 16:9-13 (emphases added), *see also* Claim 49 ("… wherein the underlying tissue site is heated to a temperature of ***40 to 80 degrees or greater***.") (emphases added), 6:3-4 ("In one embodiment the deeper dermis is heated to ***above 65 degrees*** for collagen contraction.") (emphases added), 10:30-31; Ex. 1003 ¶ 63. The disclosure in Knowlton of temperatures in the range of 40º C to 80º C encompasses the temperature range of Claim 1 of the '559 patent and renders the claimed temperature range obvious. Ex. 1003 ¶ 63. The Technomed patent describes using focused ultrasound to heat and treat varicose veins. Ex. 1007 at 5:6-10 (" The ultrasonic wave transmission means is made to transmit ultrasonic waves that are focused by the ultrasonic treatment device in said focal region with an ultrasonic intensity in the focal region of between 100 W/cm^2 and 2 kW/cm^2 for a sufficient period of time to accomplish the thermal destruction of the endothelium of the veins, leading in a few days to the thrombosis of said vein."), 2:17-21, 5:1-10, Figs. 3-4; Ex. 1003 ¶ 63. Given the proximity of varicose veins to the dermis, one skilled in the art would appreciate that treating varicose veins as described in the Technomed patent would result in the dermis being heated. Ex. 1003 ¶¶ 29, 54, 63.
to stimulate or irritate a dermis layer in the region of the skin so as to cause a change in the dermis layer of the skin that results in a change in a smoothness of an	Knowlton discloses stimulating or irritating the dermis layer under the broadest reasonable construction of Claim 1. Ex. 1003 ¶ 64. Knowlton states: "In one method of the present invention, collagen tissue in a dermis underlying the epidermis of the skin is transcutaneously contracted with the use of a thermal heating apparatus. Electromagnetic energy is transcutaneously delivered through the epidermis to the underlying dermis.

Claim 1	Knowlton/Technomed Patent
epidermis layer of the skin.	Fibroblast proliferation is initiated in the underlying dermis. Scar collagen is formed in the underlying dermis. The scar collagen is subsequently contracted and the skin is tightened." Ex. 1005 at 11:25-30. Knowlton teaches heating the dermis to temperatures disclosed in the '559 patent to cause the same biological mechanism for tightening the skin or treating wrinkles described in the '559 patent, namely causing collagen proteins to denature. *Id.* at 1:9-2:11, 4:11-14, 5:20-26, 16:9-13; Ex. 1003 ¶ 64. Knowlton states that the disclosed methods can be used for tightening the skin and treating wrinkling of the skin. Ex. 1005 at 5:13-19 ("Suitable applications for the methods of the present invention include but are not limited to, …***laxity and wrinkling of the skin***….") (emphases added), 3:16-18 ("An object of the present invention to provide [sic] a method and apparatus for tightening skin without substantially damaging the melanocytes and other epithelial cells."). Reducing or eliminating wrinkles constitutes a change in a smoothness of an epidermis layer of the skin. Ex. 1003 ¶ 64. The Technomed patent states: "The present invention essentially concerns an ultrasound apparatus for the extracorporeal therapeutic treatment of varicosities and superficial varicose veins." Ex. 1007 at 1:3-4. Treating varicose veins results in a smoothing of the skin surface by eliminating the bulging vein. Ex. 1003 ¶¶ 30, 64.

b. <u>Claim 2</u>

Claim 2	Knowlton/Technomed Patent
2. The method of claim 1, wherein a step of stimulating or irritating the dermis layer comprises elevating the	Knowlton also teaches elevating the temperature of the dermis layer. Ex. 1005 at 6:3-4 ("In one embodiment the deeper dermis is heated to above 65 degrees for collagen contraction."), 10:30-31, Claim 49 ("… wherein the underlying tissue site is heated to a temperature of 40 to 80 degrees or greater."); Ex. 1003 ¶ 65.

Claim 2	Knowlton/Technomed Patent
temperature of the dermis layer.	The Technomed patent teaches elevating the temperature of tissue to treat varicose veins. Ex. 1007 at 5:6-10 (describing use of ultrasound "to accomplish the thermal destruction of the endothelium of the veins"), 1:16-25 (describing prior art system using ultrasound to heat and treat varicose veins); Ex. 1003 ¶ 65.

As described in the claim chart above, Knowlton expressly discloses "elevating the temperature of the dermis layer." The Technomed patent further describes using focused ultrasound to heat and treat varicose veins. Given the proximity of varicose veins to the dermis, one skilled in the art would appreciate that treating varicose veins as described in the Technomed patent would result in the dermis being heated. Ex. 1003 ¶¶ 29, 54, 65.

c. Claim 3

Claim 3	Knowlton/Technomed Patent
3. The method of claim 2, wherein the step of depositing energy in the dermis layer further comprises applying the focused ultrasound beam for a time sufficient to cause proteins in the dermis layer to denature.	Knowlton states: "Electromagnetic energy may be any kind that can cause cell heating or physical destruction ***by being applied to collagen tissue***. Examples of suitable electromagnetic energy sources include, but are not limited to RF, microwave, ***ultrasound***, laser and the like." Ex. 1005 at 11:4-7 (emphases added); Ex. 1003 ¶ 66. Knowlton also discloses depositing energy in the dermis for a time sufficient to cause proteins in the dermis to denature. Ex. 1005 at 1:14-20 ("The dermis is composed mainly of extracellular protein called collagen … The phenomenon of thermal shrinkage of collagen begins with ***a denaturization of the triple helix of the collagen molecule***.") (emphases added), 12:12-15; Ex. 1003 ¶ 66. The Technomed patent describes using focused ultrasound to heat and cause the thermal destruction of

Claim 3	Knowlton/Technomed Patent
	the endothelium of a varicose vein. Ex. 1007 at 5:6-10 ("The ultrasonic wave transmission means is made to transmit ultrasonic waves that are focused by the ultrasonic treatment device in said focal region with an ultrasonic intensity in the focal region of between 100 W/cm^2 and 2 kW/cm^2 for a sufficient period of time to accomplish the thermal destruction of the endothelium of the veins, leading in a few days to the thrombosis of said vein."); Ex. 1003 ¶ 66.

As described in the claim chart above, Knowlton describes using energy, including ultrasound, to cause collagen proteins in the dermis to denature. The Technomed patent further describes using focused ultrasound to cause the thermal destruction of the endothelium of a varicose vein, which may be located within the dermis. Ex. 1003 ¶ 66. One way by which focused ultrasound results in destruction of the vein endothelium is the denaturing of proteins and enzymes caused by heating the vein. *Id.* ¶¶ 55, 66. These proteins and enzymes react to heat in a similar manner as collagen reacts. *Id.* Once a certain temperature is reached and maintained for a sufficient period of time, an irreversible change in structure occurs. *Id.*

d. Claim 4

Claim 4	Knowlton/Technomed Patent
4. The method of claim 3, wherein a step of applying a focused ultrasound beam comprises repeatedly applying	Knowlton states with respect to the described method for tightening skin and eliminating wrinkles: "***This method can be applied numerous times***. In many instances, it may be desirable to ***tighten the skin*** to a certain level and then ***in subsequent treatments*** the skin is tightened further. There may be ***four fine treatments*** to fine tune

Claim 4	Knowlton/Technomed Patent
the focused ultrasound beam over a period of days or months.	the contour effects with greater precision." Ex. 1005 at 16:2-5 (emphases added), *see also* 6:5-6 ("Sequential treatments are designed to allow for more precision in the end result."); Ex. 1003 ¶ 67.

As described in the claim chart above, Knowlton teaches that the disclosed methods may be applied over the course of multiple treatments. One skilled in the art would understand that the repeated treatments could be provided over a period of days or months. Ex. 1003 ¶ 67.

e. Claim 5

Claim 5	Knowlton/Technomed Patent
5. The method of claim 4, wherein the ultrasound beam is repeatedly applied until the wrinkles are visibly reduced.	Knowlton states: "Suitable applications for the methods of the present invention include but are not limited to, tightening and firming soft tissue, … laxity and ***wrinkling of the skin***, and the like. Wrinkling of the skin occurs as a consequence of inadequate support of the epidermis. The induction of scar collagen deposition is used for the treatment of wrinkles. Improved skin turgor is accomplished by first replenishing the collagen matrix that has been lost with aging. Following the deposition of nascent scar collagen in the dermis, contraction of collagen with a reverse thermal gradient ***corrects wrinkling of the skin***…." Ex. 1005 at 5:13-25 (emphases added); Ex. 1003 ¶ 68.

f. Claim 6

Claim 6	Knowlton/Technomed Patent
6. The method of claim 3, wherein a step of depositing energy further comprises using a	Knowlton states: "Controller 68 can also control temperature and power. An operator set level of power and/or temperature may be determined and this will not be exceeded. …. The amount of RF energy delivered controls the amount of power." Ex. 1005 at 17:21-24; Ex.

Claim 6	Knowlton/Technomed Patent
power level in the range of approximately 500 W/cm^2 to 1500 W/cm^2 at the focal point of the ultrasound beam.	1003 ¶ 69. The Technomed patent states: "…an ultrasonic treatment device is provided comprising means of focusing ultrasonic waves, defining a focal region where the ultrasonic waves are focused, and means of transmitting ultrasonic waves capable of ***producing in said focal region an ultrasonic intensity of between about 100 W/cm^2 and about 2 kW/cm^2, and preferably between 100 W/cm^2 and 500 W/cm^2***." Ex. 1007 at 2:17-21 (emphases added), *see also* 5:1-10, 11:30-12:5; Ex. 1003 ¶ 69.

As described in the claim chart above, Knowlton describes the use of controllable power levels. The Technomed patent discloses specific power levels. The disclosure in Technomed patent of power ranges between 100 W/cm^2 and about 2 kW/cm^2 encompasses the power range of Claim 6 and renders the claimed power level range obvious. *See In re Peterson*, 315 F.3d at 1330; *Galderma Labs.*, 737 F.3d at 736–41. Further, in view of the power level ranges described in the Technomed patent, which closely track the power level range in Claim 6 of the '559 patent, one skilled in the art would have found the claimed range of 500 W/cm^2 to 1500 W/cm^2 obvious. Ex. 1003 ¶ 69.

g. Claim 7

Claim 7	Knowlton/Technomed Patent
7. The method of claim 2, wherein the step of depositing energy in the dermis layer further	Knowlton discloses depositing energy in the skin, including in the dermis layer. Ex. 1005 at 11:25-27 ("In one method of the present invention, ***collagen tissue in a dermis*** underlying the epidermis of the skin is transcutaneously contracted with the use of a thermal

Claim 7	Knowlton/Technomed Patent
comprises focusing the ultrasound beam at a depth below the epidermis in a range between approximately 5 microns and 5 millimeters.	heating apparatus.") (emphases added), *see also* 1:9-18 (describing heating collagen in the dermis layer); Ex. 1003 ¶ 70. Knowlton also explains that the dermis varies in thickness throughout the body. Ex. 1005 at 1:9-13. The Technomed patent describes focusing ultrasound on varicose veins to heat and treat the veins. Ex. 1007 at cover page, 1:3-4, 2:15-21, 5:1-10; Ex. 1003 ¶ 70.

As described in the claim chart above, Knowlton describes depositing energy in the dermis. A person having skill in the art would understand that the dermis layer may be located within a range between approximately 5 microns and 5 millimeters below the epidermis. Ex. 1003 ¶ 70; Ex. 1017 at p. 376. With respect to the Technomed patent, a person skilled in the art would also understand that varicose veins may be located within a range between approximately 5 microns and 5 millimeters below the epidermis. *Id.*

h. <u>Claim 12</u>

Claim 12	Knowlton/Technomed Patent
12. The method of claim 1, wherein a step of depositing energy further comprises irritating the dermis layer without adversely damaging the epidermis layer.	Knowlton teaches: "The epidermis contains the epithelial cells and pigment forming cells called melanocytes." Ex. 1005 at 1:10-11. Knowlton further teaches: "There exists a need for skin tightening ***without damaging*** the melanocytes and other epithelial cells, or without surgical intervention." *Id.* at 3:6-7 (emphases added). Knowlton also states: "This invention relates generally to a method and apparatus for shrinking collagen containing tissue, and more particularly to a method and apparatus to shrink collagen containing tissue while creating no more than a first degree burn on an external surface." *Id.* at 1:4-7.

As described in the claim chart above, Knowlton also teaches depositing energy in the dermis layer without adversely damaging the epidermis layer. Ex. 1003 ¶ 71. Further, one skilled in the art would understand that a first degree burn, as referenced in Knowlton, is mild and does adversely damage the epidermis layer. *Id.*

i. Claim 13

Claim 13	Knowlton/Technomed Patent
13. The method of claim 12, further comprising a step of cooling the region of human skin at least one of before, during, or after depositing the ultrasound energy.	Knowlton discloses cooling the skin surface while heating the underlying collagen layers: "A reverse thermal gradient is created which cools a surface of the epidermis layer 12 while heating underlying collagen containing layers. Epidermis layer 12 as well as underlying collagen containing tissue are heated, without substantially effecting the melanocytes and other epithelial cells in epidermis layer 12, resulting in a denaturization of collagen molecules, causing a contraction of the collagen tissue and a tightening of the skin." Ex. 1005 at 15:29-16:2, *see also* 1:25-29, 5:30-31, 10:25-30, 11:8-16; Ex. 1003 ¶ 72. The Technomed patent also teaches cooling the skin in connection with the application of focused ultrasound: "Furthermore, it can be provided that the coupling liquid can be made to circulate in the means 242 at a predetermined adjustable temperature, so as to possibly produce a cooling of the surface of the patient's skin." Ex. 1007 at 13:6-8; Ex. 1003 ¶ 72.

j. Claim 14

Claim 14	Knowlton/Technomed Patent
14. The method of claim 1, wherein the region of human skin	Knowlton teaches: "Suitable applications for the methods of the present invention include but are not limited to, tightening and firming soft tissue, … laxity and ***wrinkling***

Claim 14	Knowlton/Technomed Patent
includes a wrinkle and the method further comprises the step of scanning the focused ultrasound beam over an area occupied by the wrinkle.	***of the skin***, and the like. Wrinkling of the skin occurs as a consequence of inadequate support of the epidermis. The induction of scar collagen deposition is used for the treatment of wrinkles. Improved skin turgor is accomplished by first replenishing the collagen matrix that has been lost with aging. Following the deposition of nascent scar collagen in the dermis, contraction of collagen with a reverse thermal gradient ***corrects wrinkling of the skin*** without resorting to resurfacing techniques that require the application of a standard thermal gradient burn to the skin." Ex. 1005 at 5:13-26 (emphases added).

For the reasons provided above in connection with Claim 1, Knowlton and the Technomed patent disclose the use of focused ultrasound. As described in the claim chart above, Knowlton also teaches using the disclosed methods for treating wrinkles. To heat collagen and thereby treat overlying wrinkles, the focused ultrasound is necessarily applied over and around an area occupied by the wrinkles in order to heat the underlying collagen. Ex. 1003 ¶ 73.

k. <u>Claim 15</u>

Claim 15	Knowlton/Technomed Patent
15. The method of claim 14, wherein the step of scanning further comprises scanning the focused ultrasound beam over an area of the skin that is larger than the wrinkle.	Knowlton teaches that one application for the disclosed methods is treating wrinkling of the skin. Ex. 1005 at 5:13-26; Ex. 1003 ¶ 74. Knowlton also states: "Skin tightening with a reverse thermal gradient contraction of collagen can correct areas including but not limited to the thighs, knees, arms, back and hips without unsightly scarring of standard techniques. In addition, areas previously corrected by aesthetic procedures, such as face and neck lifts, can be corrected without requiring surgery or the typical incisions around the ear." Ex. 1005 at 14:8-13; Ex. 1003 ¶ 74.

As described in the claim chart above, Knowlton teaches using the disclosed methods for treating wrinkles and identifies specific areas for treatment. Treatment of "wrinkling of the skin" requires treatment, *i.e.* applying focused ultrasound, over an area larger than the size of a single wrinkle. Ex. 1003 ¶ 74.

l. Claim 16

Claim 16	Knowlton/Technomed Patent
16. The method of claim 15, wherein the step of scanning further comprises scanning the focused ultrasound beam over an area of the skin that is approximately ten times larger than an area of the wrinkle.	Knowlton teaches that one application for the disclosed methods is treating wrinkling of the skin. Ex. 1005 at 5:13-26; Ex. 1003 ¶ 75. Knowlton also states: "Skin tightening with a reverse thermal gradient contraction of collagen can correct areas including but not limited to the thighs, knees, arms, back and hips without unsightly scarring of standard techniques. In addition, areas previously corrected by aesthetic procedures, such as face and neck lifts, can be corrected without requiring surgery or the typical incisions around the ear." Ex. 1005 at 14:8-13.

As described in the claim chart above, Knowlton teaches using the disclosed methods for treating wrinkles and identifies specific areas for treatment. Treatment of "wrinkling of the skin" and treatment over areas such as the thighs, knees, arms, back, hips, face, or neck, as identified in Knowlton, can involve scanning the focused ultrasound over an area that is approximately ten times larger than an area of a wrinkle. Ex. 1003 ¶ 75.

G. Ground 2: Obviousness of Claims 8-11 and 17-18 Over Knowlton in View of the Technomed Patent and Technomed PCT

Dependent Claims 8-11 of the ’559 patent further require inducing cavitation in the dermis layer. Claim 17 requires “depositing sufficient energy in the dermis layer to mechanically disrupt tissue to cause a dermal inflammation.” The only discussion in the ’559 patent of mechanically disrupting tissue is in connection with inducing cavitation. Ex. 1001 at 8:62-9:3. Claim 18, which depends from Claim 17, further requires “generating a shock wave to mechanically disrupt tissue in the dermis layer.” The only disclosure in the ’559 patent of generating a shock wave is in connection with a cavitational bubble collapsing and resulting in a shock wave that mechanically disrupts tissue. *Id.*; Ex. 1003 ¶ 89.

To the extent the limitations of Claims 8-11 and 17-18 are not disclosed by Knowlton or the Technomed patent, they are disclosed by Technomed PCT. Accordingly, Claims 8-11 and 17-18 would have been obvious over Knowlton in view of the Technomed patent and Technomed PCT.

1. Reasons to Combine Knowlton and the Technomed Patent with Technomed PCT

The reasons to combine Knowlton and the Technomed patent are discussed in Section V.F.1 above. It also would have been obvious for one skilled in the art to combine Knowlton and the Technomed patent with Technomed PCT. Ex. 1003 ¶¶ 76-88.

Each of the references discloses the use of ultrasound for treatment of tissue located under the skin surface. *Id.* ¶ 77. Knowlton and the Technomed patent both disclose an ultrasound device that is located external to the patient and used to treat tissue at a particular location beneath the skin surface. *Id.* ¶ 78. Technomed PCT describes the same general components. *Id.* Knowlton and the Technomed patent also disclose using ultrasound to treat issue by causing hyperthermia. *Id.* Technomed PCT also describes using focused ultrasound to heat and treat tissue. *Id.* Because the methods described in the references are so similar, one skilled in the art would appreciate that the features and components described in the references are compatible and could be combined. *Id.* ¶¶ 37, 79.

Moreover, Technomed PCT teaches that one use of the disclosed thermal and cavitation methods is the treatment of varicosities, which include varicose veins. Ex. 1009 at 8:3-5 ("Preferred current applications are … the treatment of varicosities …."). For the reasons discussed above, one skilled in the art would appreciate that the treatment of varicose veins is essentially treatment of tissue in the dermis layer. Ex. 1003 ¶¶ 29, 86. Technomed PCT also states that the disclosed methods can be used for treating skin tumors, which is a further disclosure of treating the skin. Ex. 1009 at 2:19-21. This would provide one skilled in the art further reason to combine the disclosure of Technomed PCT with Knowlton and the Technomed patent. Ex. 1003 ¶ 86.

Also, as discussed above, persons working in the field of energy based therapeutic devices would appreciate that a particular device may have a variety of potential uses or applications. *Id.* ¶ 80. One skilled in the art would have recognized that the devices and methods disclosed in Technomed PCT would have other suitable uses, particularly with respect to the treatment of similarly located tissue, such as the dermis. *Id.* Notably, Knowlton, in describing the use of focused ultrasound, cites to a secondary reference disclosing the use of focused ultrasound for treating tumors. Ex. 1005 at 15:1-8, citing Ex. 1020 ("Deep Local Hyperthermia for Cancer Therapy: External Electromagnetic and Ultrasound Techniques"). That citation in Knowlton illustrates that those working in the field appreciated that focused ultrasound could have a range of uses. Ex. 1003 ¶ 80.

Technomed PCT also teaches the use of focused ultrasound for causing cavitation, and explains that cavitation can be used in combination with hyperthermia to treat tissue. Ex. 1009 at 1:3-5 ("The present invention essentially relates to an apparatus performing therapy using ultrasound (ultrasonic therapy apparatus) that emits ultrasonic waves that produce thermal and cavitation effects."), 3:4-14, Abstract. One skilled in the art would understand that cavitation is one of the few available options for non-invasively treating tissue beneath skin and would have been motivated in view of Technomed PCT to utilize cavitation in

combination with Knowlton's disclosure of hyperthermia to cause a structural change in collagen. Ex. 1003 ¶¶ 81-82.

In addition, Knowlton explains that: "Electromagnetic energy may be any kind that can cause cell heating or physical destruction by being applied to collagen tissue." Ex. 1005 at 11:4-5. In view of Knowlton's disclosure that energy which causes physical destruction of collagen tissue may be used, one skilled in the art would have been further motivated to combine the thermal treatments described in Knowlton with cavitation, which Technomed PCT explains can be used to cause the destruction of tissue. Ex. 1009 at 1:18-21; Ex. 1003 ¶ 83.

Technomed PCT also explains benefits associated with combining hyperthermia and cavitation: "The combination of cavitation and thermal treatment has the effect of reinforcing the destructive potential of the treatment, hence limiting the duration of treatment pulses and thus avoiding heat diffusion in the tissue." Ex. 1009 at 8:13-15. One skilled in the art would appreciate that these advantages would also be applicable to the treatment of tissue for tightening skin and reducing wrinkles described in Knowlton. Ex. 1003 ¶ 84. In view of that disclosure, one skilled in the art would have been further motivated to combine the disclosure of cavitation in Technomed PCT with the disclosure of hyperthermia in Knowlton and Technomed PCT. *Id.*

In addition, the Technomed patent and Technomed PCT list two of the same inventors – Jean-Yves Chapelon and Dominique Cathignol. Exs. 1007, 1009. The Technomed patent and Technomed PCT were also published less than a year apart. In view of these commonalities, one skilled in the art would have had further reason to combine the teachings of the references. *Id.* ¶ 85.

The Technomed patent also acknowledges that ultrasound can be used to produce a thermal effect or a cavitation effect, but states that a purpose of the invention is to provide treatment primarily producing only a thermal effect with no noticeable cavitation effect. Ex. 1007 at 2:1-4. Given the recognition in the Technomed patent that ultrasound can be used to produce cavitation effects, and the further disclosure in Technomed PCT (which lists some of the same inventors as the Technomed patent) of combining thermal and cavitation effects, including for the same purpose of treating varicosities, one skilled in the art would have been motivated to combine the references. Ex. 1003 ¶ 87.

2. Differences Between the Prior Art and Claims 8-11 and 17-18 of the ’559 Patent

Knowlton and the Technomed patent do not expressly disclose inducing cavitation in the dermis layer as required by Claim 8 of the ’559 patent, and by Claims 9-11, which depend directly or indirectly from Claim 8. *Id.* ¶ 90. Knowlton and the Technomed patent also do not expressly disclose the cavitation elements of Claims 17 and 18, which are also directed to inducing cavitation.

However, Technomed PCT discloses the use of focused ultrasound for causing cavitation in tissue beneath the skin surface.

3. Claim Charts for Claims 8-11 and 17-18

The following claim charts contain specific citations to the disclosures of Knowlton, the Technomed patent, and Technomed PCT that disclose additional limitations of Claims 8-11 and 17-18 of the '559 patent. More detailed claim charts for these references are included in the accompanying declaration of Dr. Schafer. Ex. 1003 ¶¶ 91-97.

a. Claim 8

Claim 8	Knowlton/Technomed Patent/Technomed PCT
8. The method of claim 1, wherein a step of depositing energy in the dermis layer further comprises inducing cavitation in the dermis layer.	Technomed PCT describes depositing energy in tissue beneath the skin surface to induce cavitation. Ex. 1009 at 1:3-5 ("The present invention essentially relates to an apparatus performing therapy using ultrasound (ultrasonic therapy apparatus) that emits ultrasonic waves that produce thermal and ***cavitation effects***."), 1:18-21 ("***The cavitation effect*** becomes predominant when the acoustic intensity at the focal point exceeds a threshold of 150 W/cm^2. ***This cavitation effect*** is linked to the formation of microscopic gas bubbles that explode when they reach a critical diameter, thereby releasing considerable amounts of energy locally leading to the destruction of neighboring tissue.") (emphases added); Ex. 1003 ¶ 92. Technomed PCT also explains that uses of the disclosed invention include treatment of skin tumors and varicosities. Ex. 1009 at 8:1-5 ("Such a therapy apparatus according to the invention has potential uses or applications for all types of therapy using ultrasound, preferably focused, to treat all benign or malignant external or internal tumors familiar to those skilled in the

Claim 8	Knowlton/Technomed Patent/Technomed PCT
	art. Preferred current applications are the treatment of benign or malignant tumors of the liver, of the prostate, of the kidneys, of the breasts, ***of the skin*** and of the brain, ***and the treatment of varicosities*** and of the esophagus.") (emphases added); Ex. 1003 ¶ 92.

As set forth in the claim chart above, Technomed PCT discloses the use of cavitation for treatment of skin tumors and of varicosities, which includes varicose veins. Ex. 1003 ¶ 92. One of ordinary skill in the art would understand that varicose veins are located immediately beneath the skin, and may be within the dermis. *Id.* ¶¶ 30, 92. Furthermore, one skilled in the art would appreciate that during the course of treating a varicose vein as described in Technomed PCT, tissue near or surrounding the veins, including the dermis, necessarily would be targeted. *Id.*

b. <u>Claim 9</u>

Claim 9	Knowlton/Technomed Patent/Technomed PCT
9. The method of claim 8, wherein a step of depositing energy further comprises repeatedly applying the focused ultrasound beam in over a period of days or months.	Knowlton states with respect to the described method for tightening skin and eliminating wrinkles: "***This method can be applied numerous times***. In many instances, it may be desirable to ***tighten the skin*** to a certain level and then ***in subsequent treatments*** the skin is tightened further. There may be ***four fine treatments*** to fine tune the contour effects with greater precision." Ex. 1005 at 16:2-5 (emphases added), *see also* 6:5-6 ("Sequential treatments are designed to allow for more precision in the end result."); Ex. 1003 ¶ 93.

As set forth in the claim chart above, Knowlton teaches that the disclosed methods may be applied over the course of multiple treatments. One skilled in the

art would understand that the repeated treatments could be provided over a period of days or months. Ex. 1003 ¶ 93.

c. Claim 10

Claim 10	Knowlton/Technomed Patent/Technomed PCT
10. The method of claim 9, wherein the ultrasound beam is repeatedly applied until the wrinkles are visibly reduced.	Knowlton states: "Suitable applications for the methods of the present invention include but are not limited to, tightening and firming soft tissue, … laxity and ***wrinkling of the skin***, and the like. Wrinkling of the skin occurs as a consequence of inadequate support of the epidermis. The induction of scar collagen deposition is used for the treatment of wrinkles. Improved skin turgor is accomplished by first replenishing the collagen matrix that has been lost with aging. Following the deposition of nascent scar collagen in the dermis, contraction of collagen with a reverse thermal gradient ***corrects wrinkling of the skin*** …." Ex. 1005 at 5:13-26 (emphases added), *see also* 15:28-16:5; Ex. 1003 ¶ 94.

d. Claim 11

Claim 11	Knowlton/Technomed Patent/Technomed PCT
11. The method of claim 8, wherein the step of depositing energy further comprises focusing the ultrasound beam at a depth below the epidermis in a range between approximately 5 microns and 5 millimeters.	Knowlton discloses depositing energy in the skin, including in the dermis layer. Ex. 1005 at 11:25-27 ("In one method of the present invention, ***collagen tissue in a dermis*** underlying the epidermis of the skin is transcutaneously contracted with the use of a thermal heating apparatus.") (emphases added), *see also* 1:9-18 (describing heating collagen in the dermis layer). Knowlton also explains that the dermis varies in thickness throughout the body. *Id.* at 1:9-13. The Technomed patent describes focusing ultrasound on varicose veins to heat and treat the veins. Ex. 1007 at cover page, 1:3-4, 2:15-21, 5:1-10; Ex. 1003 ¶ 95. Technomed PCT also describes using focused ultrasound to treat varicosities, which include varicose veins. Ex.

Claim 11	Knowlton/Technomed Patent/Technomed PCT
	1009 at 8:3-5; Ex. 1003 ¶ 95.

As set forth in the claim chart above, Knowlton describes depositing energy in the dermis. A person having skill in the art would understand that the dermis layer may be located within a range between approximately 5 microns and 5 millimeters below the epidermis. Ex. 1003 ¶ 95; Ex. 1017 at p. 376. With respect to the Technomed patent and Technomed PCT, a person skilled in the art would also understand that varicose veins may be located within a range between approximately 5 microns and 5 millimeters below the epidermis. Ex. 1003 ¶ 95.

e. Claim 17

Claim 17	Knowlton/Technomed Patent/Technomed PCT
17. The method of claim 1, wherein a step of depositing energy in the dermis layer further comprises depositing sufficient energy in the dermis layer to mechanically disrupt tissue to cause a dermal inflammation.	Knowlton describes depositing ultrasound energy in a dermis layer. Ex. 1005 at 11:25-27 ("In one method of the present invention, collagen tissue in a dermis underlying the epidermis of the skin is transcutaneously contracted with the use of a thermal heating apparatus."); Ex. 1003 ¶ 96. Knowlton further states: "Electromagnetic energy may be any kind that can cause cell heating or physical destruction by being applied to collagen tissue." Ex. 1005 at 11:4-5; Ex. 1003 ¶ 96. Technomed PCT describes depositing energy in tissue beneath the skin surface to induce cavitation. Ex. 1009 at 1:3-5 ("The present invention essentially relates to an apparatus performing therapy using ultrasound (ultrasonic therapy apparatus) that emits ultrasonic waves that produce thermal and ***cavitation effects***.") (emphases added), 1:18-21 ("***The cavitation effect*** becomes predominant when the acoustic intensity at the focal point exceeds a threshold of 150 W/cm^2. ***This cavitation effect*** is linked to the formation of microscopic gas bubbles that

Claim 17	Knowlton/Technomed Patent/Technomed PCT
	explode when they reach a critical diameter, thereby releasing considerable amounts of energy locally leading to the destruction of neighboring tissue.") (emphases added); Ex. 1003 ¶ 96.

As set forth in the claim chart above, Technomed PCT discloses the use of ultrasound for causing cavitation and causing destruction of neighboring tissue. One skilled the in art would understand that the description in Technomed PCT of bubbles that explode and release energy to lead to the destruction of neighboring tissue constitutes a mechanical disruption of tissue. Ex. 1003 ¶ 96. One skilled in the art would also appreciate that the cavitational effect described in Technomed PCT, when used for treating the dermis, would cause a dermal inflammation resulting from energy being released into the dermis and disrupting tissue. *Id.*

f. <u>Claim 18</u>

Claim 18	Knowlton/Technomed Patent/Technomed PCT
18. The method of claim 17, wherein the step of depositing energy further comprises generating a shock wave to mechanically disrupt the tissue in the dermis layer.	Technomed PCT states: "The present invention essentially relates to an apparatus performing therapy using ultrasound (ultrasonic therapy apparatus) that emits ultrasonic waves that produce thermal and ***cavitation effects***." Ex. 1009 at 1:3-5 (emphases added). Technomed PCT also states: "***This cavitation effect*** is linked to the formation of microscopic gas bubbles that explode when they reach a critical diameter, ***thereby releasing considerable amounts of energy locally*** leading to the destruction of neighboring tissue." *Id.* at 1:19-21 (emphases added); Ex. 1003 ¶ 97.

As set forth in the claim chart above, Technomed PCT discloses the use of ultrasound for causing cavitation and causing destruction of neighboring tissue.

One skilled in the art would have understood that the mechanism by which cavitation works, including as described in Technomed PCT, involves the creation of bubbles that collapse to create a mechanical shock wave to disrupt tissue. Ex. 1003 ¶ 97. One skilled the art would have understood the description in Technomed PCT of exploding gas bubbles "releasing considerable amounts of energy locally" is referring to a shock wave. *Id.*; Ex. 1016 at p. 839.

H. Secondary Considerations, Even if Considered, Fail to Overcome the Prima Facie Evidence of Obviousness

To overcome the strong showing of obviousness set forth above, DermaFocus may attempt to present alleged secondary considerations of non-obviousness. However, secondary considerations do not support a finding of non-obviousness here.

Although secondary considerations should be taken into account, they do not control the obviousness conclusion. *Newell Cos., v. Kenney Mfg.*, 864 F.2d 757, 768 (Fed. Cir. 1988). And where a strong *prima facie* obviousness showing exists, as here, the Federal Circuit has repeatedly held that even relevant secondary considerations supported by substantial evidence may not dislodge the primary conclusion of obviousness. *See, e.g., Leapfrog Enters. Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007).

Ulthera is not aware of any secondary considerations that would be relevant to the obviousness inquiries presented here. For example, DermaFocus is a non-

practicing entity and Ulthera is not aware of any commercial success achieved by it or its predecessors in marketing or selling the alleged inventions claimed in the ’559 patent. Further, Ulthera does not believe that any potential secondary considerations could outweigh the strong *prima facie* case of obviousness. In the event that DermaFocus puts forth any allegations regarding secondary considerations of non-obviousness, Ulthera will address those allegations in due course.

VI. CONCLUSION

For the reasons set forth above, the Board should institute trial with respect to Claims 1-18 of the ’559 patent and proceed to cancel these claims as unpatentable.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 19, 2016

By: /Michelle E. Armond/
John B. Sganga, Jr.
Matthew S. Bellinger
Michelle E. Armond

Attorneys for Petitioner
ULTHERA, INC.
(949) 760-0404

CERTIFICATE OF COMPLIANCE

This document complies with the type-volume limitation of 37 C.F.R. § 42.24(a)(1)(i). This Petition contains 13,897 words, excluding the parts of the document exempted by 37 C.F.R. § 42.24(a)(1).

Dated: July 19, 2016

By: /Michelle E. Armond/
John B. Sganga, Jr.
Matthew S. Bellinger
Michelle E. Armond
Attorneys for Petitioner
ULTHERA, INC.

CERTIFICATE OF SERVICE

I hereby certify that true and correct copies of the foregoing **PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 6,113,559 AND EXHIBITS 1001-1020** are being served on July 19, 2016, via FedEx Priority Overnight on counsel of record for U.S. Pat. 6,113,559 patent owner **DermaFocus LLC**, at the address below:

Correspondence Address of Record for U.S. Pat. 6,113,559 at the U.S. Patent and Trademark Office:

Nutter, McClennen & Fish, LLP
One International Place
Boston MA 02210
ATTN: Thomas J. Engellenner, Esq.

Copies were also served on the following:

Richard E. Lyon
Sean Luner
Dovel & Luner, LLP
201 Santa Monica Blvd., Suite 600
Santa Monica, CA 90401

Dated: July 19, 2016

By: /Michelle E. Armond/
John B. Sganga, Jr.
Matthew S. Bellinger
Michelle E. Armond
Attorneys for Petitioner
ULTHERA, INC.

23450299