UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

IVANTIS, INC.,
Petitioner

v.

GLAUKOS CORP.,
Patent Owner.

U.S. Patent No.: 6,626,858
Issue Date: Sep. 30, 2003
Title: SHUNT DEVICE AND METHOD
FOR TREATING GLAUCOMA

Inter Partes Review No.: {unassigned}

PETITION FOR *INTER PARTES* REVIEW OF
U.S. PATENT NO. 6,626,858

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Exhibit 1018	Frank G. Ah-fat & Christopher R. Canning, *A comparison of the efficacy of Holmium laser sclerostomy* Ab Externo *versus trabeculectormy in the treatment of glaucoma*, 8 Eye 402 (Jul. 1, 1994)
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Exhibit 1023	Fiore, PM et al., "Use of neodymium: YAG laser to open an occluded molteno tube," Ophthalmic Surgery, 1989 May; 20(5); 373-74.

I. MANDATORY NOTICES

A. Real Party-In-Interest (§ 42.8(b)(1))

Ivantis, Inc. is the real party-in-interest for the instant petition.

B. Related Matters (§42.8(b)(2))

1. Related Litigations

On April 16, 2018, Ivantis was served with a complaint for patent infringement on U.S. Patent No. 6,626,858. The case is currently pending before the District Court for the Central District of California in the case captioned *Glaukos Corp. v. Ivantis Inc.,* Civ. Case No. 8:18- cv-00620.

2. Related Proceedings Before the Board

Petitioner is not aware of any related proceedings before the Board involving U.S. Patent No. 6,626,858.

C. Lead and Backup Counsel (§ 42.8(b)(3))

Lead Counsel	Back-up Counsel
Deborah Fishman (Reg. No. 48,621) Arnold & Porter Kaye Scholer LLP 3000 El Camino Real Five Palo Alto Square, Suite 500 Palo Alto, CA 94306-3807 T: 650-319-4500 F: 650-319-4700 deborah.fishman@arnoldporter.com	John E. Nilsson (*pro hac* motion to be filed) Paul Margulies (Reg. No. 59,580) Arnold & Porter Kaye Scholer LLP 601 Massachusetts Ave, NW Washington, DC 20001 T: 202-942-5000 F: 202-942-5999 john.nilsson@arnoldporter.com paul.margulies@arnoldporter.com
	Dorothy P. Whelan (Reg. No. 33,814) Fish & Richardson 3200 RBC Plaza

	60 South Sixth Street Minneapolis, MN 55402 T: 612-335-5070 F: 612-288-9696 whelan@fr.com

D. Service Information (§ 42.8(b)(4))

In accordance with 37 C.F.R. § 42.8(b)(4), Petitioners identify the following service information:

Deborah Fishman (Reg. No. 48,621)
Arnold & Porter Kaye Scholer LLP
3000 El Camino Real
Five Palo Alto Square, Suite 500
Palo Alto, CA 94306-3807
T: 650-319-4500
F: 650-319-4700
E: deborah.fishman@arnoldporter.com

II. PAYMENT OF FEES (37 C.F.R. § 42.103)

A payment of the required *inter partes* review fee specified in 37 C.F.R. § 42.15(a) is being paid at the time of filing of this petition. If there are any additional fees due in connection with the filing of this paper, please charge the required fees to our Deposit Account No. 502387.

III. REQUIREMENTS FOR IPR (37 C.F.R. § 42.104)

A. CERTIFICATION OF GROUNDS FOR STANDING

As required by 37 C.F.R. § 42.104(a), Petitioner certifies that the patent for which review is sought is available for *inter partes* review and that

Petitioner is not barred or estopped from requesting an *inter partes* review on the grounds identified herein.

B. IDENTIFICATION OF CHALLENGED CLAIMS AND STATEMENT OF THE PRECISE RELIEF REQUESTED

Petitioner respectfully requests *inter partes* review under 35 U.S.C. §§ 311-318 and 37 C.F.R §§ 42.100-42.123, and the cancellation of claims 24–27, 30, 33–36, 40, 47, 48, and 50 of U.S. Patent No. 6,626,858 (the "'858 patent") (Ex. 1001) for the following reasons:

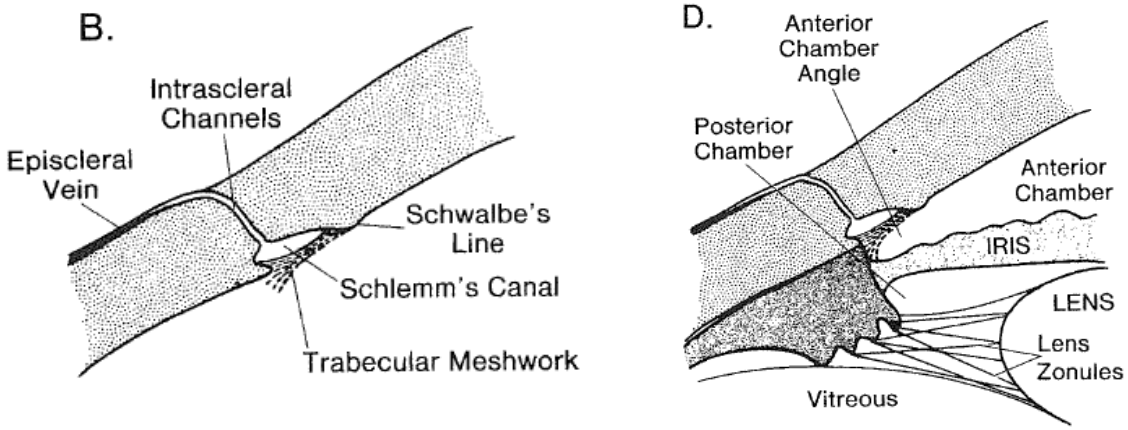
(i) Claims 24-27, 30, 34, 40, 47 and 48 of the '858 patent are rendered obvious under 35 U.S.C. § 103 by Detlev Spiegel, *Surgical Glaucoma Therapy*, *in* Benefits and Risks of Ophthalmological Therapy: Main Presentations of the 33rd Essen Continued Education for Ophthalmologists 79-82 (Herausgegeben von Anselm Kampik & Franz Grehn ed., 1998) ("Spiegel") (Ex. 1003, certified translation) in view of Australian Patent Application Publication No. 199876197 B2 ("Grieshaber") (Ex. 1004).

(iii) Claims 33, 35, 36 and 50 are rendered obvious under 35 U.S.C. § 103 by Spiegel (Ex. 1003) in view of Grieshaber (Ex. 1004) in further view of U.S. Patent No. 5,868,697 ("Richter") (Ex. 1005).

The reasons for unpatentability, and specific evidence supporting this request are detailed below and in the supporting Declaration of Dr. Andrew Iwach, M.D. (Ex. 1006).

IV. BACKGROUND ANATOMY AND TECHNOLOGY

The '858 patent is directed to the treatment of glaucoma, an eye disease linked to elevated intraocular pressure. Ex. 1006 ¶ 21. Elevated intraocular pressure stems from the build-up in the eye of a fluid called "aqueous humor," which is produced by ciliary bodies located in the posterior chamber of the eye. *Id.* ¶¶ 13-15. The relevant anatomy of the eye is shown below:



Id. ¶ 15. Generally, aqueous humor flows into the anterior chamber of the eye and drains out in large part through the "canalicular" route. *Id.* ¶ 14. In passing through this route, aqueous humor flows from the anterior chamber of the eye, across the trabecular meshwork, and into a structure encircling

the cornea known as Schlemm's canal. *Id.* Aqueous humor then drains out of the eye through collecting channels located on the outer wall of Schlemm's canal that connect to the episcleral venous system, as depicted in the figure below. *Id.*

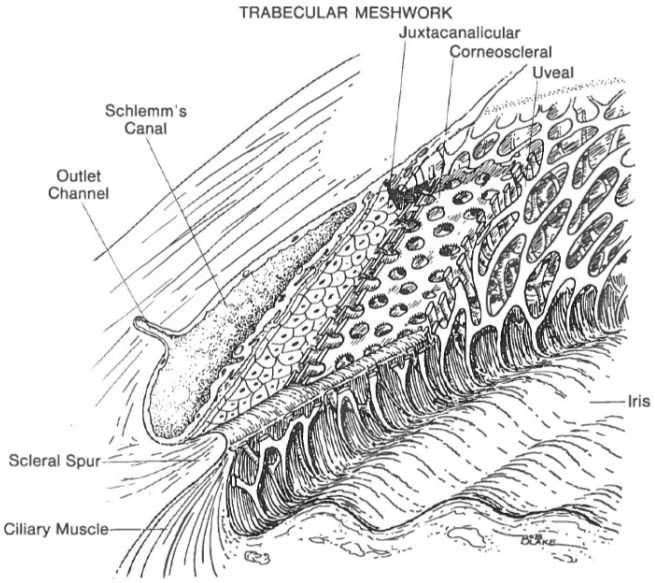


Figure 2.10. Three layers of trabecular meshwork (shown in cutaway views): (1) uveal; (2) corneoscleral; and (3) juxtacanalicular.

Id. ¶ 15.

Schlemm's canal is a fragile, tube-like structure that follows the circumference of the cornea. *Id.* ¶ 16. The ring formed by the canal is approximately 36 mm in circumference, with a radius of approximately 5.7 mm. *Id.* The interior diameter of the canal averages 190-370 μm. Ex. 1007 at 15. The average thickness of the trabecular meshwork near the scleral spur is 120 μm. Ex. 1011 at 272. The diameter of each trabecular hole is highly variable, as is the space between each layer of the trabeculum. *Id.*

In eyes afflicted with glaucoma, this process of natural outflow is compromised, leading to a decrease in the outflow of aqueous humor and a consequent increase in intraocular pressure. Ex. 1006 ¶ 17. If left untreated, the intraocular pressure may rise, which may result in optic nerve damage, blindness, and severe pain. *Id.*; Ex. 1005 at 1:16-25. Treatments for glaucoma have thus focused on relieving intraocular pressure, whether through medication, laser treatments, or surgery. Ex. 1006 ¶ 18.

By 1999, it was well-known that increased resistance at the trabecular meshwork was a major cause of decreased outflow of aqueous humor from eyes afflicted with glaucoma. Ex. 1006 ¶ 18. For decades before the filing date of the '858 patent, surgeons had addressed congenital pediatric glaucoma or uveitic glaucoma by removing or bypassing the trabecular meshwork and providing direct access to Schlemm's canal using minimally invasive glaucoma surgery. *Id.* For example, surgeons frequently utilized trabeculectomy and trabecular bypass surgeries to enhance the aqueous humor outflow and reduce intraocular pressure ("IOP"). *Id.*; *see also* Ex. 1007 at 569-70; Ex. 1018 at 402. In a trabeculectomy procedure, a type of filtration surgery, a surgeon creates a new route for aqueous humor to flow out of the anterior chamber through angle structures and into sub-conjunctival space. Ex. 1006 ¶ 18; Ex. 1005 at 1:32-41. Although

trabeculectomy had been a mainstay in glaucoma surgery since the 1960s, the limitations and shortcomings of this technique were widely known before 1999. Ex. 1006 ¶ 18; *see also* Ex. 1003 at 83. For instance, the blebs (drainage sites) created by this procedure put the eye at long-term risk of infection with the possibility of a resulting loss in vision. Ex. 1006 ¶ 18.

Accordingly, other treatments developed, including the surgical implantation of glaucoma drainage devices, to bypass the trabecular meshwork and facilitate drainage of aqueous humor from the anterior chamber. Ex. 1006 ¶ 18; *see, e.g.*, Ex. 1013 at 28; Ex. 1019 at 120; Ex. 1014 at 571-572; Ex. 1017 at 339.

Even with minimally-invasive surgical techniques, tissue obstruction, including iris tissue obstruction, was a known complication with the implantation of glaucoma drainage devices. More specifically, by 1999, iris prolapse was reported as a common complication of glaucoma drainage surgery. Ex. 1006 ¶ 20. Likewise, it was also recognized in the art by 1999 that draining devices and passageways could be obstructed or compromised by fibrosis (or scarring). *Id*.

V. OVERVIEW OF THE ’858 PATENT AND ITS PROSECUTION HISTORY

The ’858 patent issued on September 30, 2003 and, on its face, claims priority to U.S. Provisional Patent App. No. 60/131,030 (the “’030

provisional"), which was filed on April 26, 1999. The '858 patent issued as a continuation of U.S. Application No. 08/558,505, filed on April 26, 2000, which claims priority to the '030 provisional application and which later issued as U.S. Patent No. 6,450,984.[1]

The '858 patent is directed to a shunt device and method for continuously decompressing elevated intraocular pressure by diverting aqueous humor from the anterior chamber of the eye into Schlemm's canal and the natural outflow pathways of the eye. Ex. 1001 at 1:12-19; *see also id.* at Abstract, 5:14-25. The '858 patent acknowledges that, at the time of filing, it was known that the primary pathway for aqueous outflow in humans is through the "canalicular" route—*i.e.*, from the anterior chamber across the trabecular meshwork, into Schlemm's canal and out through the collecting channels that drain into the episcleral venous system of the eye. *Id.* at 1:47-2:5. The '858 patent also notes that "[i]n primary open angle glaucoma, which is the most common form of glaucoma, the abnormal resistance [through the canalicular outflow system] is believed to be along the outer aspect of the trabecular meshwork and the inner wall of Schlemm's canal." *Id.* at 2:10-13.

[1] *See* Ex. 1001 at Related U.S. Application Data.

The ’858 patent acknowledges that “[t]he prior art includes a number of . . . aqueous shunt devices” directed at placing an aqueous diversion device within the anterior chamber to drain aqueous humor to, for instance, the corneal surface; and the scleral, conjunctival, and subconjunctival spaces. Ex. 1001 at 4:17-27. Additionally, the ’858 patent notes that “[s]ome prior art references for glaucoma management have been directed at Schlemm’s canal” and that increasing the flow of aqueous humor across the trabecular meshwork can be used to control intraocular pressure. Ex. 1001 at 4:17-46. For example, the ‘858 patent recognizes that the prior art includes devices for “inject[ing] a viscous material [into Schlemm’s canal] to hydraulically expand and hydrodissect the trabecular meshwork.” *Id.*

VI. OVERVIEW OF THE PRIOR ART

As discussed above, the ’858 patent acknowledges that the prior art taught to manage glaucoma by focusing on/opening up Schlemm’s canal and the trabecular meshwork. Ex. 1001 at 4:39-40. In fact, it was understood in the art, and acknowledged by the ’858 patent, that drainage problems with the trabecular meshwork contributed to elevated intraocular pressure and glaucoma and, thus, the trabecular meshwork was a well-recognized focus for treating elevated intraocular pressure and glaucoma. *Id.* at 2:10-16; *see also* Ex. 1004 at 1a, 5; Ex. 1003 at 81; Ex. 1005 at 1:27-30. It was also

known in the art for decades before the filing date of the '858 patent that intraocular pressure and glaucoma, particularly congenital pediatric glaucoma or uveitic glaucoma, could be addressed by removing or bypassing the trabecular meshwork and providing access directly to Schlemm's canal using minimally invasive glaucoma surgery. Ex. 1006 ¶¶ 18-19. Moreover, contrary to the assertion in the '858 patent, indwelling implants for Schlemm's canal to facilitate improved drainage of aqueous humor across the trabecular meshwork and to the outflow collector channels were also known in the prior art. *Id*. ¶ 20.

A. Detlev Spiegel, *Surgical Glaucoma Therapy, in* Benefits and Risks of Ophthalmological Therapy: Main Presentations of the 33rd Essen Continued Education for Ophthalmologists

The Spiegel book chapter was published on or before August 1998, at least 6 months before the priority date of the '858 patent, and was publicly available by October 1998. Ex. 1008 ¶ 5. As such, the Spiegel reference is prior art under 35 U.S.C. § 102(a). While Spiegel was submitted as prior art in an Information Disclosure Statement by the applicant, it was never cited by the Examiner and did not form the basis for any rejection during prosecution.[2]

[2] *See* Ex. 1009 at 110, 11/29/02 Information Disclosure Statement ("IDS"). Spiegel was also submitted in parent application of the '858 patent, U.S.
(continued...)

In the Introduction, Spiegel notes that there were two approaches in the art to reduce intraocular pressure by surgical methods: (1) "reduc[e] production of aqueous humor by cyclodestructive procedures" (thereby destroying the ciliary bodies); and (2) "increas[e] aqueous outflow." Ex. 1003 at 79. Spiegel states that the increase in aqueous outflow or drainage "can be achieved by either improving aqueous outflow via the existing outflow pathways, or by creating a new outflow pathway that connects the anterior chamber with the subconjunctival space." *Id.*

Spiegel teaches that "[t]reating the cause of glaucoma requires improving aqueous outflow via existing outflow pathways." *Id.* at 80. Spiegel then describes a number of approaches in the art for improving aqueous humor drainage via existing channels: "This can be accomplished by surgical iridectomy, argon laser trabeculoplasty, selective laser trabeculoplasty, trabeculotomy, as well as by experimental methods of viscocanalostomy and drainage of Schlemm's canal." *Id.*

App. No. 09/558,505, first in an IDS (where it was not cited by the Examiner and did not form the basis for any rejection) and later, after notice of allowance, by a third party pursuant to 37 C.F.R. §1.291. Ex. 1010 at 307-11. However, the protest was filed after a notice of allowance and was never addressed by the Examiner.

Spiegel recognizes that the trabecular meshwork is often responsible for the increase in intraocular pressure: "The increase in intraocular pressure … is generally believed to be caused by a decrease in the ability of trabecular meshwork to facilitate aqueous outflow due to pathological changes." Ex. 1003 at 81. Moreover, Spiegel recognizes that the best solution for this reduced drainage across the trabecular meshwork is to bypass the trabecular meshwork and connect the anterior chamber directly to Schlemm's canal: "The optimal solution to this problem would be to bypass the trabecular meshwork and create a direct connection from the anterior chamber into the aqueous veins, which would allow for [decreased pressure] resulting from outflow through Schlemm's canal." *Id*.

To that end, Spiegel describes placing an indwelling shunt into Schlemm's canal at one end with the other end of the shunt in the anterior chamber for the purpose of improving aqueous humor drainage from the anterior chamber into the eye's natural outflow drainage channels. Ex. 1003 at 81. Specifically, Speigel describes "insert[ing] a silicone tube with an outer diameter of 150 μm through a scleral flap incised into Schlemm's canal" wherein "[o]ne end of the tube [is] seated in Schlemm's canal" and "the other end [is] slid into the anterior chamber once the inner wall of Schlemm's canal [is] opened." *Id.*

Spiegel Figure 7.1 depicts a tube inserted into Schlemm's canal, while Figure 7.2 shows the positioning of the other end of the tube inside the anterior chamber of the eye. *See* Ex. 1003 at 82.

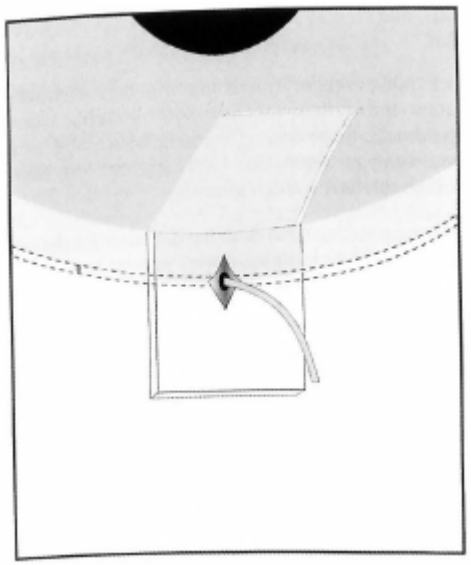


Figure 7.1

Figure 7.2

Although clinical application in live patients had not yet been made, Spiegel describes testing this improved aqueous humor drainage method and device on cadaverous eyes. Ex. 1003 at 81-82.

B. Australian Patent Application Publication AU 199876197 ("Grieshaber")

The Grieshaber Australian patent application was published on February 25, 1999, two months before the priority date of the '858 patent and, as such, constitutes prior art under 35 U.S.C. § 102(a). *See* Ex. 1004.

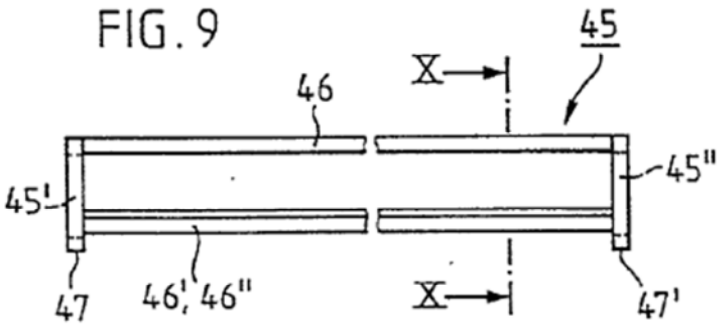
Grieshaber describes an indwelling ocular stent, implanted within Schlemm's canal, to treat glaucoma by facilitating aqueous humor drainage along the canalicular outflow pathway. Specifically, Grieshaber notes, "[t]he present invention relates to a method and to a device to improve aqueous humor drainage in an eye, by which the aqueous humor secreted by the ciliary body is drained in the region of the iridocorneal angle through the trabecular meshwork into the canal of Schlemm and from there through the subsequent natural outflow pathways." Ex. 1004 at 1a. Grieshaber discloses "a support element (35) subsequently implanted in the lumen (16) of the canal of Schlemm, the inner walls of the canal are supported and permanently held in an expanded position, whereby unimpeded drainage of the aqueous humor from the canal of Schlemm through the subsequent outflow pathways (20) is ensured." Ex. 1004 at Abstract.

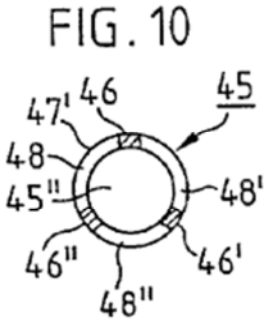
Additionally, Grieshaber describes methods for treating changes in the trabecular meshwork that may "completely or only partially obstruct the drainage of the aqueous humor" into Schlemm's canal. Ex. 1004 at 1a. For

instance, Grieshaber teaches the injection of a substance such as hyaluronic acid "so that the trabecular meshwork is hydraulically expanded and its pores are opened" to reestablish passage of aqueous humor across the trabecular meshwork (from the anterior chamber) and into Schlemm's canal. Ex. 1004 at 1a.

Like the devices claimed in the '858 patent, Grieshaber's implants are designed to treat intraocular pressure by maintaining the patency of Schlemm's canal. *Compare* Ex. 1001 at 9:20-22 ("The shunt device 100 can also help to maintain the patency of Schlemm's canal in a stenting fashion.") *with* Ex. 1004 at 2 ("the present invention provides an axially oriented support element which supports the inner wall of the canal of Schlemm in the region of the locally expanded lumen and which is placed such that the aqueous humor can permanently drain from the canal of Schlemm through the subsequent natural outflow pathways of the eye.").

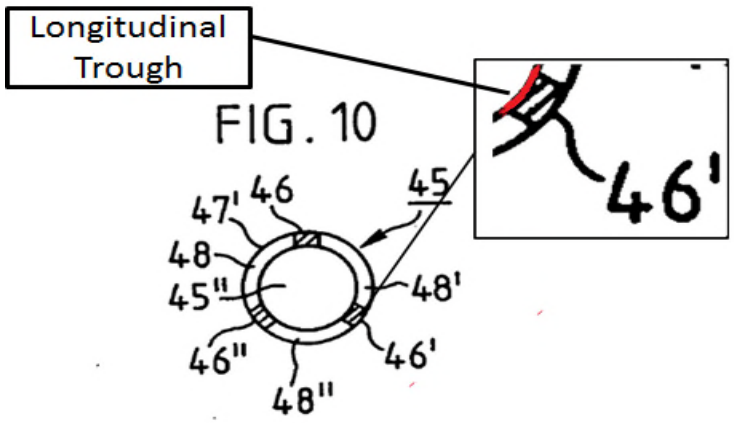
Grieshaber describes several embodiments of an ocular stent, one of which includes a "substantially hollow cylindrical support element." Ex. 1004 at 8, 10. One embodiment is shown in Figures 9 and 10 below:





The overall device of Figures 9 and 10 is the "support element 45." Ex. 1004 at 8. At one end is "opening 45'" and at the other is "opening 45"." *Id.* at 8. These openings are defined by "end portions 47, 47'," which are comprised of "axially spaced toruses"—rings—that are linked to each other by "two, but preferably three webs 46, 46', and 46" placed circumferentially at intervals…." *Id.* Those portions marked 48, 48', and 48" represent open gaps or "recesses" designed to "serve . . . as outflow openings for the aqueous humor to be drained…." *Id.* In other words, the implant is formed of two rings ("toruses" designated 45' and 45") linked by longitudinally extending pieces ("webs" designated 46, 46' and 46"). The gaps between these narrow pieces ("recesses" designated 48, 48' and 48") are open so as to allow drainage of aqueous humor from the trabecular meshwork to Schlemm's canal and the natural outflow pathways of the eye. Ex. 1006 ¶ 44. The body of the device is "curved" longitudinally to approximate the curvature of Schlemm's canal. Ex. 1004 at 9 ("In a variant embodiment not

depicted, there is also the possibility that the support element 35; 40; 45; 50 or 55 is designed longitudinally somewhat arcuate."); Ex. 1006 ¶ 44. The radial curve of the Figure 9 & 10 embodiment defines the "trough-like" interior of the longitudinal "webs," designated 46', as shown below:



See also Ex. 1006 ¶ 45.

Grieshaber also discloses a Figure 4 and Figure 7 embodiment, which comprise a support element (35) with a long tube (36) that contains a number of throughholes (38, 38'). Grieshaber teaches that the support element 35 is preferably positioned and implanted in Schlemm's canal so that "at least one of the throughholes 38, 38' connects with the small collector channels 21', 22' of the natural outflow pathways 20'." Ex. 1004 at 6-7. Figures 4 and 7, shown below, depict this alignment of openings to collector channels:

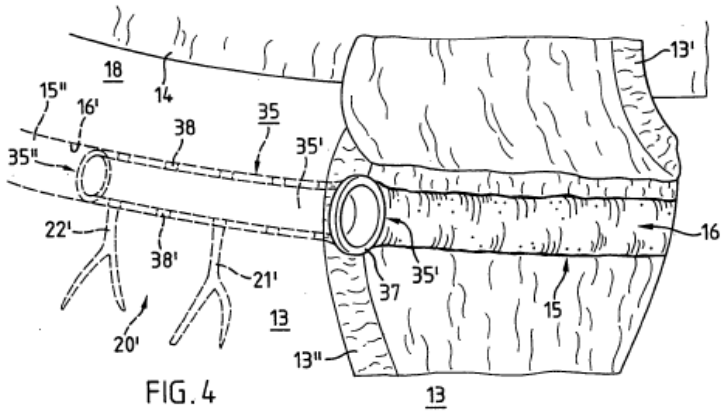


FIG. 4

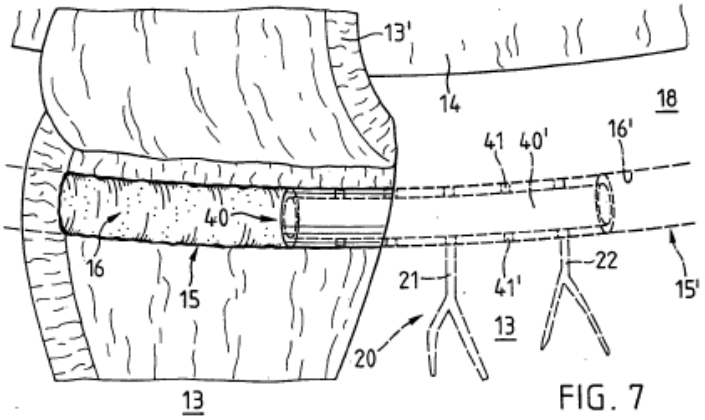


FIG. 7

Grieshaber reports that "[t]he aqueous humor penetrating through the trabecular meshwork 18 exits through the canal of Schlemm 15 or through the interior 40' of the support element 40 and through the openings 41' and collector channels 21, 22 of the subsequent natural outflow pathways." Ex. 1004 at 7. Grieshaber's Figure 5 provides additional detail on the pipe (36) or tube of support element (35) described in Figures 4 and 7 above. The proximal end (35') is fitted with a "collar" (37) to prevent displacement of the implant in Schlemm's canal. Ex. 1004 at 6.

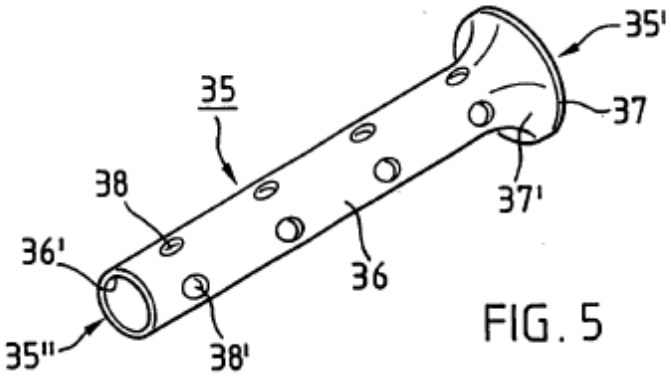


FIG. 5

The implant also possesses "throughholes" (designated 38 and 38'), or fenestrations, which are "distributed axially and circumferentially" along its body and "connect[] with the small collector channels . . . of the natural outflow pathways." *Id.* at 6-7.

Grieshaber also discloses embodiments with support elements formed of braids of mesh or helical coils. For instance, Figure 11 (shown below) depicts "a helicoidal network made of threads designed to be interlinked and advantageously stiff." Ex. 1004 at 8. The gaps in this mesh (52 and 52') "serve respectively as outflow opening for the aqueous humor." *Id.*

FIG. 11

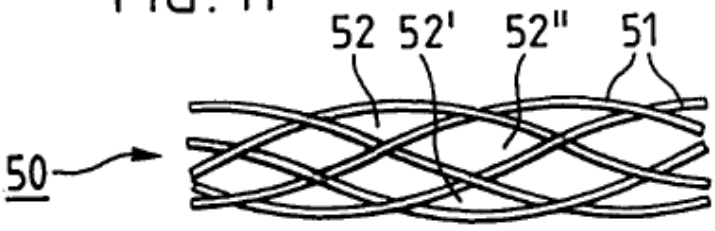
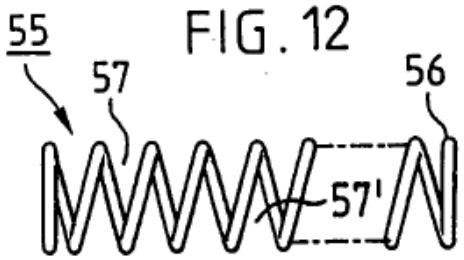


Figure 12 (shown below) depicts an embodiment in which the support element is formed of a single wire (56) wound in a helix shape. *Id.* at 9.



"In this variant, the gaps 57 and 57' provided between the individual turns serve respectively as outflow openings for the aqueous humor." *Id.*

Grieshaber makes clear that the support element in each of these embodiments serves as a scaffold to hold open Schlemm's canal and to permit aqueous to travel from the anterior chamber, across the trabecular meshwork through Schlemm's canal and to the subsequent natural outflow pathways (collector channels and episcleral veins): "With the support element 35 or 40, the lumen 16 of the canal of Schlemm 15 is permanently held open …. The aqueous humor penetrating into the trabecular meshwork 18 exits via the canal of Schlemm 15 or via the lumen 36' or 40' of the support element 35 or 40 and via the openings 38' or 41' and collector channels 21', 22' or 21, 22 of the subsequent natural outflow pathways 20' or 20." *Id.* at 11; *see also* Figs. 4 and 7. Thus, Grieshaber teaches various configurations of stents that facilitate aqueous humor flow from the

trabecular meshwork, into Schlemm's canal, and out through collector channels and the natural outflow openings of the eye.

C. U.S. Patent No. 5,868,697 ("Richter")

Richter constitutes prior art under both 35 U.S.C. §§ 102 (a) and (e) because it issued on February 9, 1999 from U.S. Application No. 08/623,238, which was filed on March 27, 1996. *See* Ex. 1005.

Richter states that the "goal of glaucoma treatment is to reduce the IOP [intraocular pressure] to a level which is considered safe for a particular eye, but which is not so low as to cause ocular malfunction or retinal complications." Ex. 1005 at 1:27-30. To that end, Richter describes an ocular shunt that enters the anterior chamber from the sclera. *Id*. at 4:61-5:9.

Richter notes that ocular implants "tend to clog over time, either from the inside by tissue, such as the iris, being sucked into the inlet or from the outside by the proliferation of cells, for example by scarring." Ex. 1005 at 2:13-16. Richter teaches design solutions to minimize such obstruction. *Id*. at 5:50-60. For instance, Richter teaches that the "inlet end" of the shunt placed within the anterior chamber has as an "angled" tip with a "beveled surface" to "increase[] the area of the axial inlet 41 to enlarge the entrance of the tube passage 38." *Id.* at 5:50-54. Furthermore, the beveled surface

should be "designed to face away from the iris 22 to reduce the possibility of obstruction of the axial inlet 41." *Id.* at 5:54-56.

Richter notes that the "goal of glaucoma treatment is to reduce the IOP to a level which is considered safe for a particular eye, but which is not so low as to cause ocular malfunction or retinal complications." Ex. 1004 at 1:27-30. Richter also teaches that the internal diameter of the shunt should be "sufficiently small to prevent flow when the IOP is below a threshold amount" in order to prevent hypotony. Ex. 1005 at 2:48-49, 5:21-27. For instance, an exemplary embodiment has a "cylindrical tube passage 38" with a "diameter of about 300 micrometers." *Id*. at 5:23-24.

VII. GROUNDS FOR UNPATENTABILITY

A. Person of Ordinary Skill in the Art

The '858 patent acknowledges that the prior art teaches aqueous shunt devices for glaucoma and glaucoma surgery directed to Schlemm's canal. *See* Ex. 1001 at 4:17-46. The claimed inventions are aqueous shunts with particular characteristics. Accordingly, one of ordinary skill in the art would have either (1) a medical degree and at least two years' experience in ophthalmology; or (2) an undergraduate or graduate degree in biomedical or mechanical engineering and at least two years of work experience, including familiarity with ophthalmic anatomy. *See* Ex. 1006 ¶ 31.

B. Claims 24-27, 30, 34, 40, 47 and 48 are Obvious Based on Spiegel in View of Grieshaber

Spiegel teaches a tube that passes from the anterior chamber through the trabecular meshwork to divert aqueous humor from the anterior chamber of the eye into Schlemm's canal. *See supra* Section VI(A). Grieshaber describes an ocular implant that is inserted into Schlemm's canal to maintain the patency of the canal and to facilitate the drainage of aqueous humor from the trabecular meshwork across Schlemm's canal and out to the collecting channels of the eye. Ex. 1004 at 2:21-25; *see also supra* Section VI(B). Grieshaber explicitly states that: "[t]he present invention relates to a method and to a device to improve aqueous humor drainage in an eye, by which the aqueous humor secreted by the ciliary body is drained in the region of the iridocorneal angle through the trabecular meshwork into the canal of Schlemm and from there through the subsequent natural outflow pathways." *Id.* at 1a-2.

Both Spiegel and Grieshaber recognize the importance of enhancing flow through the trabecular meshwork and into Schlemm's canal, thereby facilitating the flow of aqueous humor from the anterior chamber to the natural outflow pathways. For example, Grieshaber teaches that the drainage of aqueous humor may be impeded by changes in the trabecular meshwork "which [] completely or only partially obstruct the drainage of the

aqueous humor." Ex. 1004 at 1a-2. Spiegel, meanwhile, teaches that a silicone tube can be used to improve aqueous humor drainage by "seat[ing one end of the tube] in Schlemm's canal while the other end [is] slid into the anterior chamber once the inner wall of Schlemm's canal [is] opened." Ex. 1003 at 81. Thus, both Spiegel and Grieshaber address the same problem and propose the same solution — an implant in Schlemm's canal that allows for enhanced drainage out of the canal and into the natural collecting channels of the eye. Ex. 1006 ¶ 55.

One of ordinary skill in the art would have been motivated to use the teachings of Grieshaber, which provides various designs for a Schlemm's canal implant, to modify or design the shunt of Spiegel, which teaches a flexible tube inserted into Schlemm's canal. Ex. 1006 ¶¶ 55-56. Moreover, one of ordinary skill in the art would have had a reasonable expectation of success in combining Spiegel with Grieshaber, since the modifications suggested by Grieshaber to Spiegel are simple design choices in the fabrication of the shunt. Ex. 1006 ¶¶ 56, 64

1. Independent Claim 24

Claim 24 is an independent claim that recites:

> *An aqueous humor shunt device to divert aqueous humor in an eye from the anterior chamber into Schlemm's canal, the shunt device comprising*

a distal portion having at least one terminal aspect sized and shaped to be received within a portion of Schlemm's canal and

a proximal portion having at least one terminal aspect sized and shaped to be received within the anterior chamber of the eye,

wherein device permits fluid communication from the proximal portion in the anterior chamber to the distal portion in Schlemm's canal,

wherein the shunt device is non-linear prior to insertion.

This claim would have been obvious to one of ordinary skill in the art before the '858 patent filing based on the teachings of Spiegel in view of Grieshaber.

a. "An aqueous humor shunt device to divert aqueous humor in an eye from the anterior chamber into Schlemm's canal, the shunt device comprising"

Spiegel teaches that "the optimal solution" to address impaired aqueous humor drainage "would be to bypass the trabecular meshwork and create a direct connection from the anterior chamber into the aqueous veins, which would allow for [decreased pressure] resulting from outflow through Schlemm's canal." Ex. 1003 at 81. To achieve this, Spiegel discloses that a silicone tube can be used to improve aqueous humor drainage by positioning "[o]ne end of the tube [ ] in Schlemm's canal, while the other end [is] slid into the anterior chamber once the inner wall of Schlemm's canal [is]

opened." *Id*. Spiegel explains that this shunt may be used to "improv[e] aqueous outflow via existing outflow pathways." *Id*. As noted above, the natural flow for aqueous humor is from the anterior chamber, through the trabecular meshwork, and into Schlemm's canal. *See supra* Section IV. Thus, Spiegel teaches bypassing the trabecular meshwork by using a shunt device that diverts aqueous humor from the anterior chamber into Schlemm's canal.

b. "a distal portion having at least one terminal aspect sized and shaped to be received within a portion of Schlemm's canal"

Spiegel teaches inserting a tube having an "outer diameter of 150 μm" (or 0.15 mm)[3] into Schlemm's canal. Ex. 1003 at 81. For a shunt to be sized and shaped to be received within a portion of Schlemm's canal, it must have a diameter that is no larger than the diameter of Schlemm's canal because if a shunt were to have too large a diameter, there would be a risk of tearing Schlemm's canal, a delicate structure, during insertion. Ex. 1006 ¶ 60.

It was known in the art that the diameter of Schlemm's canal is between approximately 190-370 μm, or 0.19-0.37 mm. *See* Ex. 1006 ¶ 60;

[3] This is the diameter along its entire length, including at its "terminal aspect." Ex. 1006 ¶ 61.

Ex. 1007 [Chapter 2, p.15]. Thus, a tube with a diameter slightly smaller than that of Schlemm's canal, such as Spiegel's tube with an external diameter of 0.15mm, would be "sized and shaped to be received within a portion of Schlemm's canal." Ex. 1006 ¶ 61.

c. "a proximal portion having at least one terminal aspect sized and shaped to be received within the anterior chamber of the eye"

As noted above, one end of Speigel's shunt is "seated in Schlemm's canal, while the other end [is] slid into the anterior chamber[.]" Ex. 1003 at 81. This is illustrated by the arrow Spiegel provides in Figure 7.2, indicating the end of the shunt protruding slightly into the anterior chamber:

Ex. 1003 at 82; Ex. 1006 ¶ 62. The "terminal aspect" of the tube of Spiegel is thus "sized and shaped to be received within the anterior chamber of the eye." Ex. 1006 ¶ 62.

d. "wherein device permits fluid communication from the proximal portion in the anterior chamber to the distal portion in Schlemm's canal"

Spiegel teaches that the insertion of a silicone tube into both Schlemm's canal and the anterior chamber may be used to "improve aqueous outflow via existing outflow pathways." Ex. 1003 at 81. As noted above, Spiegel teaches an implant where "[o]ne end of the tube [is] seated in Schlemm's canal, while the other end [is] slid into the anterior chamber" to facilitate the drainage of aqueous humor. *Id*. Aqueous humor flows into the tube at the end placed in the anterior chamber and exits into Schlemm's canal at the other end. Ex. 1006 ¶ 63. Thus, Spiegel discloses a device that 'permits fluid communication from proximal portion in the anterior chamber to the distal portion in Schlemm's canal." *Id*.

e. "wherein the shunt device is non-linear prior to insertion"

As was known in the art, Schlemm's canal is a circular structure with a natural curvature. *See supra* Section IV. One of ordinary skill would have recognized that, to fit within Schlemm's canal, an implant should have a shape that contours the natural curvature of Schlemm's canal. Ex. 1006 ¶ 64. Indeed, during prosecution, the Examiner noted that "[a]n engineer designing a shunt device to 'fit' within Schlemm's canal for implantation would realize the shunt device should approximate the curvature of

Schlemm's canal so that no unnecessary stress is placed upon the walls of Schlemm's canal." Ex. 1009 at 146, 1/29/2003 Rejection at 6.

One of ordinary skill would have recognized that a shunt device designed to fit within Schlemm's canal could be made of a flexible material that adapts to the natural curvature of Schlemm's canal upon insertion or, alternatively, could be designed with a pre-formed curvature approximating the curvature of Schlemm's canal. Ex. 1006 ¶ 64. Indeed, during prosecution, the Examiner expressly recognized these two possible design choices:

> An engineer designing a shunt device to "fit" within Schlemm's canal for implantation would realize the shunt device should approximate the curvature of Schlemm's canal so that no unnecessary stress is placed upon the walls of Schlemm's canal. Also, knowing the curvature of Schlemm's canal differs in individuals, the engineer would fabricate the shunt device from a flexible material so that the shunt device can be adapted to virtually every individual. Therefore, it would have been an obvious engineering expedient at the time the invention was made to one having ordinary skill in the art to manufacture the shunt device of U.S. Patent No. 6,450,984 with a preset radius of curvature (non-linear) approximating the most common radius of curvature of Schlemm's canal for the purpose of allowing the shunt device to be well-received in Schlemm's canal. Furthermore, to adapt the shunt device to eyes having a radius of curvature slightly different than the preset radius of curvature, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to make the shunt device from a flexible material for the purpose of

> allowing the shunt device to "fit" into various sized Schlemm's canals.

Ex. 1009 at 144, 1/29/2003 Rejection at 6.

One of ordinary skill would have known that the silicone shunt of Spiegel could be made either from flexible silicone that would adapt to Schlemm's upon insertion or could be pre-formed from more rigid silicone with a curvature that approximates the shape of Schlemm's canal. Ex. 1006 ¶¶ 64-67. Either way, it would have been obvious that the silicone shunt of Spiegel could have been "non-linear prior to insertion."[4]

In any event, one of ordinary skill would have recognized that a non-linear shunt with a preformed curvature prior to insertion was also obvious based on Spiegel in view of Grieshaber. Ex. 1006 ¶¶ 66. Grieshaber expressly discloses using a preformed curvature as an alternative to a flexible stent or shunt for insertion into Schlemm's canal. Ex. 1004 at 9. Grieshaber teaches that a Schlemm's canal implant may be "designed, for example, as tubes or spirals made of suitable biocompatible material enable, in particular, due to their inherent flexibility, optimal adaptation to the natural shape of the canal of Schlemm 15," or that "[i]n a variant not

[4] One of ordinary skill would have appreciated that a flexible silicone shunt could be (and often would be) "non-linear" before insertion.

depicted, there is also the possibility that the support element 35; 40; 45; 50 or 55 is designed longitudinally somewhat arcuate," or curved. *Id.*

Thus, one of ordinary skill in the art would have had reason to employ a shunt that was "non-linear prior to insertion" — either a non-linear flexible tube or a shunt with a preformed curvature — because those were two known design choices for an implant that could be inserted into and reside within Schlemm's canal. Ex. 1006 ¶ 64. Where, as here, there exists a finite set of options (two) that will work for a given problem — to design a shunt for insertion into Schlemm's canal — it would be obvious for one of ordinary skill to try that predictable option. *Bayer Schering Pharma A.G. v. Barr Labs., Inc.*, 575 F.3d 1341 (Fed. Cir. 2009)

Furthermore, one of ordinary skill would have had a reasonable expectation of success in employing either a flexible or a pre-formed curvature design, like that disclosed in Grieshaber, as both designs were known in the art. Ex. 1006 ¶ 64. Moreover, there was nothing unpredictable in designing a shunt with a preformed curvature, rather than using an inherently flexible material, and there is no reason to expect that either design choice would impede the functionality of the claimed stent. *Id*. *See, e.g., Depuy Spine, Inc. v. Medtronic Sofamor Danek, Inc*., 567 F.3d 1314 (Fed. Cir. 2009). It would have been obvious to use a shunt that is non-

linear prior to insertion, particularly a non-linear shunt approximating the natural curvature of Schlemm's canal. Ex. 1006 ¶ 67.

Thus, claim 24 is rendered obvious based on Spiegel in view of Grieshaber.

2. Claims 25 and 34

Claims 25 and 34 depend from Claim 24 and recites the additional respective limitations:

Claim 25	**Claim 34**
wherein said distal portion of the shunt has an outer diameter of about 0.1mm and to 0.5 mm *and a length of about 1 mm to 20 mm,* *and wherein said proximal portion has a length of about 0.1 mm to 3 mm.*	*wherein said distal portion has an outer diameter of about 0.30 mm.*

The '858 patent describes the distal portion as "sized and shaped to be circumferentially received within a portion of Schlemm's canal." Ex. 1001 at 6:54-56; *see also id.* at 13:27-29 (claim 24).

a. *Claim 25 - "wherein said distal portion of the shunt has an outer diameter of about 0.1 mm and to 0.5 mm"*

As discussed above, Spiegel teaches the insertion of a "silicone tube with an outer diameter of 150 μm [0.15 mm] through a scleral flap incised

into Schlemm's canal." Ex. 1003 at 81. Grieshaber notes that "the support elements have . . . an external diameter D = 0.2 mm," which is between 0.1 mm and 0.5 mm. Ex. 1004 at 9. Both Spiegel and Grieshaber therefore teach a distal portion that has an outer diameter between 0.1 mm and 0.5 mm. Ex. 1006 ¶ 70.

b. Claim 25 - "wherein said distal portion of the shunt has . . . a length of about 1 mm to 20 mm"

Claim 25 adds the limitation that the distal portion of the shunt of Claim 24 has a "*length of about 1 mm to 20 mm*." Grieshaber discloses that the "support elements have, for example, a length L = 2.0 mm," which is between 1 mm and 20 mm. Ex. 1004 at 9. Thus, claim 25 is rendered obvious by the combination of Speigel and Grieshaber. Ex. 1006 ¶ 71.

c. Claim 25 - "wherein said proximal portion has a length of about 0.1 mm to 3 mm"

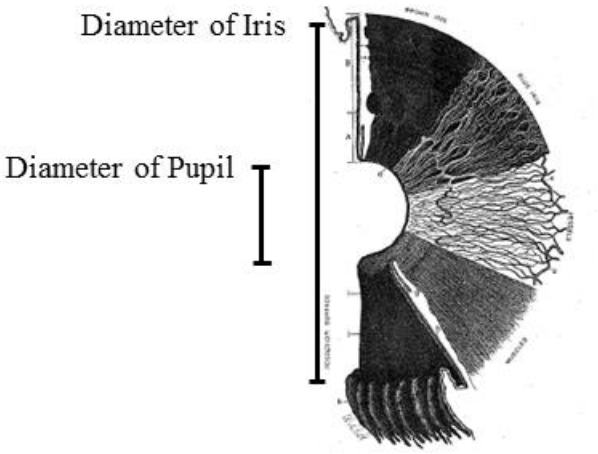
Claim 25 also requires that the proximal portion of the shunt of Claim 24 (the portion residing in the anterior chamber) have "*a length of about 0.1 mm to 3 mm*." A shunt having a proximal portion length within this range would have been obvious to an ordinarily skilled artisan due to the limitations imposed by the anatomy of the human eye. Ex. 1006 ¶¶ 72-73.

As explained by the '858 patent, "[t]he proximal portion 10 is preferably of sufficient length, about 0.1 to 3 mm or about 2.0 mm, to extend

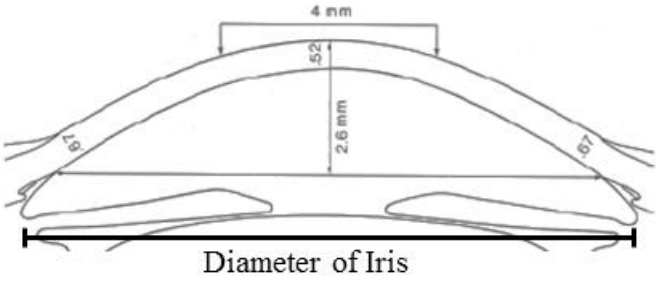
from its junction with the distal portion 25 in Schlemm's canal towards the adjacent space of the anterior chamber." Ex. 1001 at 10:5-8. Consistent with this, at a minimum, the proximal portion should extend through the entire trabeculum to establish direct fluid communication between the anterior chamber and Schlemm's canal. Ex. 1006 ¶ 72. The average thickness of the trabecular meshwork is roughly 120 μm, or .12 mm. Ex. 1006 ¶ 72.; Ex. 1011 at 272. Accordingly, designing a proximal portion to have a minimum length of about 0.1 mm would have been obvious to one of ordinary skill in the art. Ex. 1006 ¶ 72.

In addition, one of ordinary skill in the art would also have known that the length of the proximal portion of an implanted shunt is limited by the space between the cornea and the iris, the length of the iris from the angle to the pupil, and the depth of the anterior chamber. Ex. 1006 ¶ 73. It well-known in the art that a shunt must be inserted far enough into the angle of the anterior chamber so that it would not be so close to the iris that it could be occluded by the tissue of the iris. Ex. 1006 ¶ 73; Ex. 1005 at 2:13-16; Ex. 1013 at 32; Ex. 1014 at 572. Indeed, iris prolapse into drainage pathways formed by surgical or laser trabeculectomy was well-documented in the literature. Ex. 1006 ¶ 73; Ex. 1005 at 1:60-62; Ex. 1018 at 402.

Likewise, the length of a proximal portion of a shunt (protruding into the anterior chamber) should also be limited by the length of the iris from angle to pupil. As illustrated below, the average radius of the iris—which expands and contracts—was known to be approximately 6 mm. Ex. 1006 ¶ 73; Ex. 1015 at 205 ("The diameter of the iris is about 12 mm."). One of ordinary skill would know that limiting the length of the proximal portion of the shunt to about 3 mm would ensure that the shunt would not extend into the pupil and visual axis of the eye. Ex. 1006 ¶ 73.



Ex. 1015 at 207 (annotated).



Ex. 1015 at 61 (annotated with the diameter of the iris).

Moreover, a shunt with a proximal portion that is too long could contact the cornea, thereby causing corneal damage. Ex. 1006 ¶ 74. Corneal contact (or abrasion) was a known source of clinical complications following glaucoma drainage device implantation. *Id*.; Ex. 1016 at 203. Glaucoma implants and procedures were therefore developed to minimize this risk. *See* Ex. 1006 ¶ 74; Ex. 1019 at 122.

These anatomical considerations would lead one of ordinary skill in the art to use a proximal portion having a length of "about 0.1 mm to 3 mm." Ex. 1006 ¶ 75. In fact, similarly dimensioned glaucoma treatment implants were known in the art. *Id*.; Ex. 1017 at 340; Ex. 1019 at 122. Thus, in light for the forgoing, a shunt with a proximal portion having a length of about 0.1 mm to 3.0 mm would have been obvious to an ordinarily skilled artisan. Ex. 1006 ¶ 76.

d. Claim 34

Claim 34 also depends from independent claim 24, but adds the limitation "*wherein said distal portion has an outer diameter of about 0.30 mm.*" The word "about" in a claim limitation "avoids a strict numerical boundary to the specified parameter." *Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd.*, 476 F.3d 1321, 1326-1327 (Fed. Cir. 2007). "[H]ow far beyond the claimed range the term 'about' extends a patent claim" depends

"on the criticality of the numerical limitation of the invention." *Id.* (citations omitted). Nothing in the '858 patent or its file history suggests that "0.30mm" is a critical parameter of claim 34. Therefore, Grieshaber's (Ex. 1004 at 9) disclosure of an implant with an outer diameter of 0.2 mm, discussed above with respect to claim 25, also renders obvious claim 34 because 0.2 mm is "about 0.3 mm."

The '858 patent states that "[t]he diameter of width of the distal portion 25 can be sized to yield an outer diameter of between about 0.1 and 0.5 mm, or about 0.3 mm, for a tubular or curved shunt . . . ." Ex. 1001 at 10:64-67. Neither the patent nor the prosecution history gives any indication that 0.3 mm might be critical. To the contrary, during prosecution, the Examiner expressly recognized that the recited external diameter and recited length were not critical parameters of the claimed invention: "Applicants have not disclosed that a 0.1 mm to 0.5 mm diameter and a 1 to 20 mm length provides an advantage, is used for a particular purpose, or solves a stated problem." Ex. 1009 at 130, 12/20/2002 Rejection at 5-6. Thus, one of ordinary skill in the art would have appreciated that there is no significant difference between Grieshaber's outer diameter of 0.2 mm and the recited outer diameter of 0.3 mm. Ex. 1006 ¶ 85.

In any event, it would have been obvious to design the shunt of Claim 24 to include a distal portion with an outer diameter of about 0.30 mm. First, to the extent that an outer diameter of "about 0.30 mm" is different than an outer diameter of 0.2 mm, the difference is an obvious matter of design choice with no functional difference. Ex. 1006 ¶¶ 83-86. Moreover, designing a shunt with an external diameter of "about 0.30 mm" would have been obvious to an ordinarily skilled artisan in view of the anatomical dimensions of Schlemm's canal. As discussed above, it was known in the art that Schlemm's canal has a diameter of between approximately 190-370 μm (0.19-.37 mm). Ex. 1007 [Chapter 2, page 15]. One of ordinary skill would have known that the external diameter of the portion of the shunt designed for axial insertion into Schlemm's canal should not be larger than the diameter of Schlemm's canal. *See* Ex. 1006 ¶ 87. Thus, it would have been obvious to one of ordinary skill to design the distal portion of a shunt for insertion into Schlemm's canal with an outer diameter of about 0.30 mm. In fact, the Examiner noted during prosecution that "manufacturing the distal portion to have an outer diameter of about 0.30 mm is also a design choice following the rationale above, since in order for the device to be placed into Schlemm's canal, certain dimensions of the distal portion must be maintained." Ex. 1009 at 148, 1/29/2003 Rejection at 8; *see also id.*at

130,12/20/2002 Rejection at 5-6 (noting that the dependent claim "merely recites a more specific outer diameter dimension (0.30 mm) of the distal portion, which is included in the range of 0.1 to 0.5 mm").

Thus, claim 34 would have been obvious to one of ordinary skill in the art based on Spiegel in view of Grieshaber.

3. Claims 26 and 27

Claim 26 depends from Claim 24 and recites the additional limitation "*wherein said distal portion has a curve having a radius which approximates the radius of Schlemm's canal of a human eye, wherein the radius is between about 3 mm and 10 mm.*" Claim 27 depends from Claim 26 and recites the additional limitation, "*wherein said curve has a radius of about 6 mm.*"

Grieshaber teaches that the Schlemm's support element may be "made of a suitable biocompatible material" and must "enable, in particular, due to their inherent flexibility, optimal adaptation to the natural shape of the canal of Schlemm 15." Ex. 1004 at 9. It was known in the art at the time of patent filing that the radius of Schlemm's canal was approximately 6.0 mm in a typical human eye. Ex. 1001 at 10:54; Ex. 1006 ¶ 80; Ex. 1015 at 138 ("The ring formed by the canal measures 36 mm. in circumference[.]").

One of ordinary skill in the art would have understood that a shunt that adopts the natural shape of Schlemm's canal would have a radius of approximately 6.0 mm, which is between 3 mm and 10 mm. *See* Ex. 1006 ¶ 82. As noted by the Examiner during prosecution, "it would have been obvious to shape the distal portion of the shunt device to approximate the radius of Schlemm's canal in human eye (claim 49), which is 6 mm (claim 50) for the purpose of inserting the device into Schlemm's canal." Ex. 1009 at 130. Moreover, Spiegel, which teaches using a tube made of silicone, an inherently flexible material, is in accord. *See* Ex. 1003 at 81. Thus, the combination of Spiegel and Grieshaber renders obvious claims 26 and 27.

4. Claim 30

Dependent Claim 30 recites the shunt device of Claim 24 and adds the following limitation: "*wherein the distal portion extends in one direction within Schlemm's canal*."

Spiegel teaches that "[o]ne end of the tube was seated in Schlemm's canal, while the other end was slid into the anterior chamber once the inner wall of Schlemm's canal was opened." Ex. 1003 at 81. The shunt of Spiegel extends in only one direction within Schlemm's canal (from the point of insertion into Schlemm's canal), not unlike the shunt depicted in

Figure 5A of the ’858 patent. *See* Ex. 1006 ¶ 82. Thus, claim 30 would have been obvious based on Spiegel in view of Grieshaber.

5. Claim 40

Claim 40 depends from Claim 24 and recites the additional limitation, “*wherein the distal portion has one or more fenestrations therein that allow the passage of fluid into Schlemm’s canal*.”

The ’858 patent uses the term “fenestration” to describe the opening 20 in Figure 5B and openings 15 and 30 in Figure 2. Ex. 1001 at 6:16-20, 8:23-26, 9:20-25. The ’858 patent notes that “fenestrations may be of any functional size, and circular or non-circular in various embodiments of the present inventions.” Ex. 1001 at 10:29-31. Additionally, “[a]ll or parts of the device may be solid, porous, tubular, trough-like, fenestrated, or pre-curved.” Ex. 1001 at 7:53-54. One of ordinary skill in the art reading the term “fenestration” in the context of the ’858 patent would therefore understand it to mean “an opening.” *See also* Ex. 1006 ¶ 88.

Grieshaber discloses ocular implants for placement within Schlemm’s canal with openings that comprise fenestrations to allow fluid into Schlemm’s canal. Figures 4-8 of Grieshaber depict an embodiment with “a number of throughholes 38, 38’ distributed axially and circumferentially spaced.” Ex. 1004 at 6. Figures 4-7 and 8 of Grieshaber depict “outflow

opening" 41 facing trabecular meshwork 18. Ex. 1004 at 6-8. The outflow openings are "spaced at intervals axially and arbitrarily distributed circumferentially or placed diametrically opposite each other and connected with the interior 40'." Ex. 1004 at 7-8. Similarly, the recesses of Figures 9 and 10 of Grieshaber "serve in each case as outflow openings." Ex. 1004 at 8. Grieshaber explains that "[t]he aqueous humor penetrating through the trabecular meshwork 18 exits through the canal of Schlemm . . . ." Ex. 1004 at 7. Thus, claim 40 is rendered obvious by Spiegel and Grieshaber. Ex. 1006 ¶¶ 87-89.

6. Claim 47

Dependent Claim 47 recites the shunt device of Claim 24 and adds the following limitation: "*wherein at least a portion of the distal portion is selected from the group consisting of a round tubular channel, an ovoid tubular channel, a semi-tubular channel, and a partially open trough-like channel*." A "Markush claim" is a type of patent claim that lists alternative elements that can be included in the claim and satisfying any one of these claim elements is sufficient for purposes of anticipation and/or obviousness. *See Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 334 F.3d 1274, 1281 (Fed. Cir. 2003).

The ’858 patent alternatively refers to the aqueous humor shunt device as a “aqueous humor directing channel” and notes that “[t]he invention contemplates many different configurations for an aqueous humor directing channel….For example, the aqueous humor directing channel can be a fully enclosed lumen, a partially enclosed lumen, or a trough-like channel that is at least partially open.” Ex. 1001 at 7:13-20. The ’858 patent further recognizes that “[t]ubular channels can be round, ovoid, or any other enclosed geometry.” Ex. 1001 at 8:41-42.

Spiegel teaches the insertion of a “tube” (i.e. “tubular channel”) in Schlemm’s canal. Ex. 1003 at 81. As shown in Figure 7.1 and 7.2, the tube is round or circular.

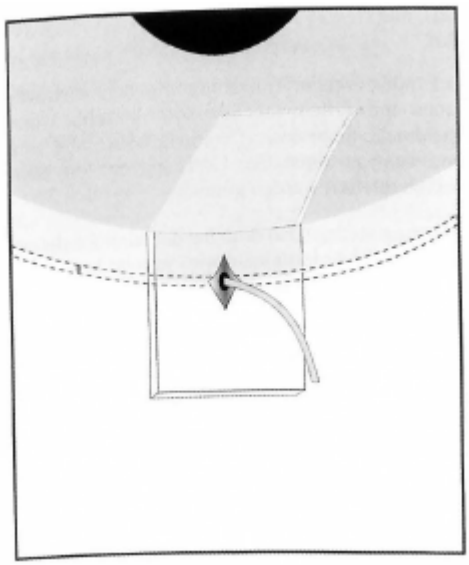


Figure 7.1

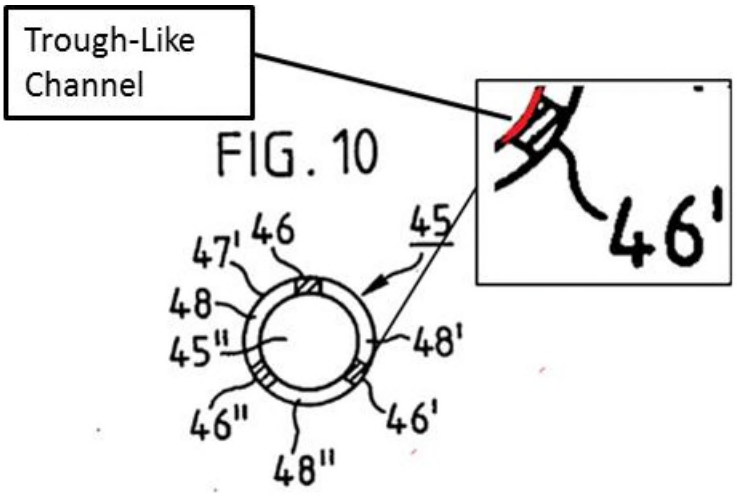
Figure 7.2

Thus, Claim 47 is rendered obvious by Spiegel. Ex. 1006 ¶¶ 90-91.

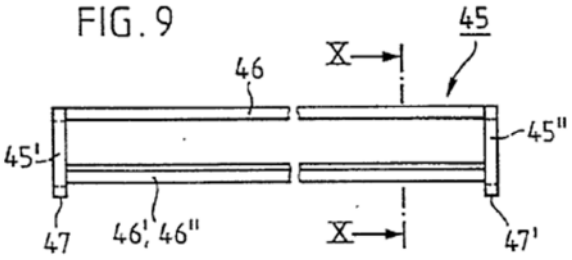
7. Claim 48

Claim 48 depends from Claim 24 and recites the additional limitation, "*wherein at least a portion of the distal portion is a partially open trough-like channel open posteriorly toward one or more collecting channels of the eye.*"

Grieshaber Figures 9 and 10 disclose an implant with longitudinal webs or panels arranged along the circumference of two round end pieces. Ex. 1004 at 8. As depicted in Figure 10, this arrangement creates an arcuate depression or channel along the length of the web:



This depression or channel forms a trough that extends from end to end, as shown in Figure 9:



Additionally, each web lies opposite one of the "recesses 48, 48', and 48", which "serve in each case as outflow openings for the aqueous humor to be drained substantially through the openings 45' and 45"." *Id.*

In addition, with respect to the stents depicted in Figures 4 and 7, Grieshaber teaches implanting the stent such that "at least one of the outflow openings 38, 38' or 41, 41' . . . is connected with the collector channels 21', 22' or 21, 22 of the subsequent natural outflow pathways 20' or 20." Ex.

1004 at 11. Grieshaber's teaching likewise applies to position the recesses, or outflow openings 48, 48' and 48" identified in Figures 9 and 10, to face the collecting channels along the posterior wall of Schlemm's canal and maximize aqueous fluid flow from Schlemm's to the natural outflow pathways of the eye. *See id.* at 8. As shown in Figs. 9 and 10 above, the webs are oriented to face towards an opening in the support element and, when the stent is implanted in Schlemm's canal, at least one opening or recess in the support element will open towards the collecting channels in the posterior wall of Schlemm's canal. Ex. 1006 ¶¶ 92-95.

Thus, Claim 48 would have been obvious based on the combination of Spiegel and Grieshaber.

C. Claims 33, 35, 36, and 50 are Rendered Obvious by Spiegel in View of Grieshaber in Further View of Richter

As discussed above, it would have been obvious to combine the shunt of Spiegel, which extends from the anterior chamber across the trabecular meshwork and into Schlemm's canal, with Grieshaber, which teaches a Schlemm's canal implant for increasing fluid flow across the trabecular meshwork and into the collecting channels of the eye.

One of ordinary skill in the art would have been similarly motivated to combine the teachings of Spiegel with Richter because Richter discloses

design information to avoid a known problem for the proximal end of Spiegel's shunt, which resides in the anterior chamber.

By April of 1999, it was well-known in the art that ophthalmic implants placed within the anterior chamber may become clogged and fail because the "[r]apid aqueous escape" from the anterior chamber "creates a relative vacuum anterior to the iris," causing the iris to be sucked into the opening of the implant, thereby blocking it. Ex. 1012 at Abstract; Ex. 1006 ¶¶ 99-101; Ex. 1014 at 572 (recording implant complications, including "[t]ube blockage with . . . iris"). This phenomenon is also recognized by the '858 patent: "Because the nature of the iris 40 is such that it tends to comprise a plurality of rather flaccid fimbriae of tissue, it is desirable to avoid said fimbriae from being drawn into the lumen of an implant, thus occluding the shunt device." Ex. 1001 at 10:18-21.

Richter, too, recognized this problem, explaining that implants "suffer from several disadvantages," including that they "tend to clog over time, either from the inside by tissue, such as the iris, being sucked into the inlet, or from the outside by the proliferation of cells, for example by scarring." Ex. 1005 at 2:8-9, 2:13-16. Richter teaches that the end of the tube or shunt placed within the anterior chamber should have a "beveled surface 36 designed to face away from the iris 22 to reduce the possibility of

obstruction of the axial inlet 41." Ex. 1005 at 5:54-56. Thus, one of skill in the art would appreciate that the teaching of Richter may be applied to solve a known problem with shunts inserted into the anterior chamber, such as Spiegel. Moreover, because Richter's solution (a beveled surface to the implant) is a simple matter of design choice, one of ordinary skill in the art would have had a reasonable expectation of success in modifying the shunt of Spiegel at the proximal end with the design of Richter. Ex. 1006 ¶ 100.

1. Claims 35 and 36

Claims 35 depends from Claim 24 and recites the additional limitation, "*wherein said proximal portion is tubular having a lumen with an internal diameter of between about 0.1 mm and 0.5 mm*." Claim 36 also depends from Claim 24 and recites the following additional limitation, "*wherein said proximal portion is tubular with a lumen with an internal diameter of about 0.2 mm*."

Spiegel teaches the use of a shunt comprised of a "silicone tube with an outer diameter of 150 μm," which is 0.15 mm. Ex. 1003 at 81. One of ordinary skill in the art would have understood that the internal diameter of the tube would be slightly smaller, such as around 0.1 mm, as claimed. Ex. 1006 ¶ 102.

In addition, Richter recognizes that the interior diameter of a tube exiting the anterior chamber of the eye must have "a cross-sectional area sufficiently small to inhibit the flow of aqueous humor through the tube passage." Ex. 1005 at 5:21-23. Richter teaches that "using a specified internal cross-sectional area for the tube passage," such as a "cylindrical tube passage 38 has a diameter of about 300 micrometers", or about 0.3 mm, may prevent excessive loss of aqueous humor from the eyeball. Ex. 1005 at 5:23-27.

Neither the '858 patent nor its prosecution history disclose any advantage, particular purpose, or rationale for this claimed range. *See* Ex. 1001 at 10:9-13. Thus, one of skill in the art would have been motivated to design the portion of a shunt placed within the anterior chamber to have an internal diameter between about 0.1 mm and 0.5 mm, and claim 35 is rendered obvious by Spiegel, Grieshaber, and Richter. Ex. 1006 ¶¶ 102-105.

It also would have been obvious for one of ordinary skill in the art to design a shunt with an internal diameter of about 0.2 mm. As noted above, the claim limitation "about" serves to "avoid[] a strict numerical boundary to the specified parameter." *Ortho-McNeil*, 476 F. 3d at 1326-27. "When determining how far beyond the claimed range the term 'about' extends a patent claim," the focus should be "on the criticality of the numerical

limitation to the invention." *Id.* at 1327. In other words, one should determine the purpose of the limitation, and determine how much a given element can deviate from that limitation and still serve the same purpose. *See Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1368 (Fed. Cir. 2008).

While the specification of the '858 patent notes that "the proximal portion 10 can be sized to yield an internal diameter of between 0.1 mm and 0.5 mm, but preferably 0.20 mm," it gives no indication for why 0.20 mm is preferred. One of ordinary skill in the art would have therefore recognized that 0.20 mm is not critical and that a tube with an internal diameter of 0.1 mm, as with Spiegel, or 0.3 mm, as with Richter, would meet the claim limitation of "about 0.2 mm." Ex. 1006 ¶¶ 104-105. Thus, claim 36 is rendered obvious by the combination of Spiegel and Grieshaber in further view of Richter.

2. Claim 33

Claim 33 depends from Claim 24 and recites the additional limitation, "*wherein the proximal portion extends from the distal portion at an angle to avoid occlusion from contact with corneal endothelium tissue or iris tissue when the distal portion is located within Schlemm's canal.*"

The specification of the ’858 patent notes that the “the proximal portion 10 joins the distal portion(s) 25 at an angle sufficient to allow the placement of the proximal portion 15 within the anterior chamber of the eye when the distal portion 25 is oriented in the plane of Schlemm’s canal.” Ex. 1001 at 10:1-5. Additionally, the ’858 patent states that “the inventive device is designed so that placement of the distal portion 25 within Schlemm’s canal 30 results in an orientation of the proximal portion 10 within the anterior chamber 35 within the angle defined by the iris 40 and the inner surface of the cornea 45.” Ex. 1001 at 11:32-36.

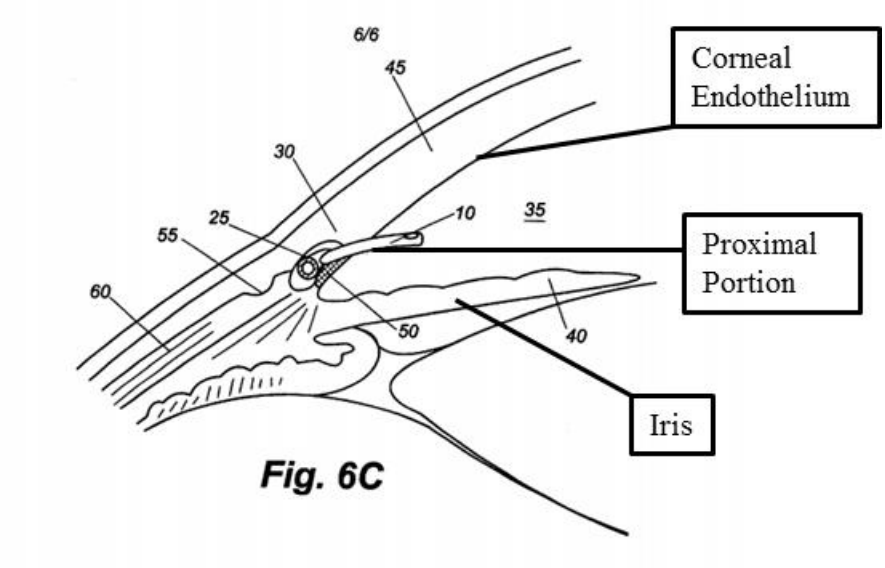
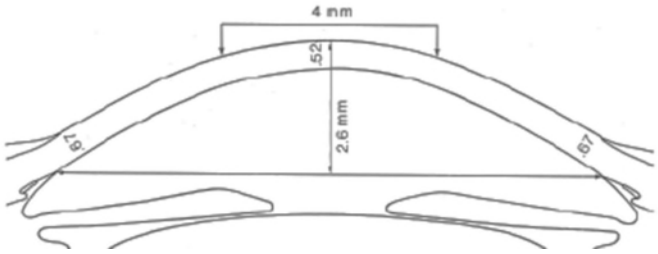


Fig. 6C

As discussed above, Richter also recognizes the need to place a shunt appropriately between the iris and cornea in the anterior chamber. Richter explains that implants “suffer from several disadvantages,” including that they “tend to clog over time, either from the inside by tissue, such as the iris,

being sucked into the inlet, or from the outside by the proliferation of cells, for example by scarring." Ex. 1005 at 2:8-9, 2:13-16. One of ordinary skill in the art would have known that the positioning of the proximal portion of an implanted shunt is constrained by the anatomy of cornea and the iris. Ex. 1006 ¶ 108; *see supra* VII(C)(1)(a) (claim 25).



Ex. 1015 at 61. One of ordinary skill would have understood further that the proximal portion of the shunt, which enters the anterior chamber, should extend from the distal portion to enter the anterior chamber at an angle that avoids the iris (occlusion) and the cornea (abrasion). Ex. 1006 ¶ 108.

Thus, claim 33 is rendered obvious by the combination of Spiegel and Grieshaber in further view of Richter.

3. Claim 50

Claim 50 depends from Claim 24 and recites the additional limitation, "*in which the terminal aspect of the proximal portion is angled internally towards the anterior chamber with respect to the proximal portion.*" In one embodiment of the '858 patent, shown in Figure 2, "the terminal aspect 16

of the proximal portion is angulated *toward the iris* 40 with respect to the main axis of the proximal portion 10." Ex. 1001 at 8:27-31 (emphasis added). However, the '858 patent explains that, "[i]n alternate embodiments, as shown in FIG. 6C, the portal 18 of the proximal portion 16 is directed *away from the iris* 40." *Id.*at 8:32-34 (emphasis added).

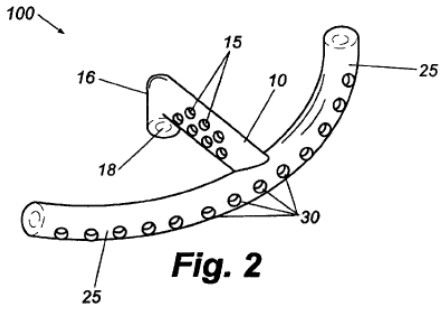


Fig. 2

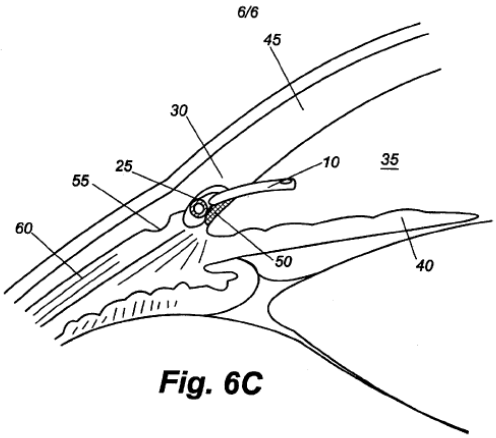


Fig. 6C

In such embodiments, "portal 18 [is] oriented anteriorly to face away from the underlying iris 40." Ex. 1001 at 10:38-43. The patent recognizes that "[s]uch a configuration would tend to decrease the possibility of occlusion of the shunt device by the iris 40." *Id.* at 10:43-45.

Richter teaches that ocular implants "tend to clog over time, either from the inside by tissue, such as the iris, being sucked into the inlet or from the outside by the proliferation of cells, for example by scarring." Ex. 1005 at 2:13-16. Richter therefore discloses that the "inlet end" of the shunt placed within the anterior chamber has as an "angled" tip with a "beveled

surface" to "increase[] the area of the axial inlet 41 to enlarge the entrance of the tube passage 38." Ex. 1005 at 5:50-54. The beveled surface should be "designed to face away from the iris 22 to reduce the possibility of obstruction of the axial inlet 41." Ex. 1005 at 5:54-56. The "beveled surface 36 lies in a plane which is angled opposite to the plane in which disk 34 lies," which is the proximal portion of Richter. Ex. 1005 at 5:58-60; Ex. 1006 ¶ 112. Thus, Richter discloses an ocular implant that is angled internally towards the anterior chamber and which includes a portal (i.e. a beveled opening 174) that opens anteriorly away from the iris to avoid occlusion. *Compare* Ex. 1001 at Fig. 6C *with* Ex. 1005 at Fig. 13; Ex. 1006 ¶ 112.

Given the anatomical constraints of the angle structure as well as the known problem of iris occlusion, one of ordinary skill in the art would have been motivated to modify the shunt of Spiegel so that its "terminal aspect of the proximal portion is angled internally towards the anterior chamber with respect to the proximal portion," in accordance with Richter. Ex. 1006 ¶ 112. Thus, claim 50 is rendered obvious by the combination of Spiegel, Grieshaber, and Richter.

VIII. CONCLUSION

For the foregoing reasons, claims 24-27, 30, 33-36, 40, 47-48, and 50 of the '858 patent are each unpatentable under 35 U.S.C. § 103. Petitioner therefore requests that an *inter partes* review of these claims be instituted.

Date: May 23, 2018

Respectfully submitted,

/DEBORAH E. FISHMAN/

Deborah Fishman (Reg. No. 48,621)
Arnold & Porter Kaye Scholer LLP
3000 El Camino Real
Five Palo Alto Square, Suite 500
Palo Alto, CA 94306-3807
T: 650-319-4500
F: 650-319-4700
E: deborah.fishman@apks.com

Attorney for Petitioner

CERTIFICATE OF WORD COUNT

Pursuant to 37 C.F.R. § 42.24 (d), I certify that the present paper contains 10,202 words as counted by the word-processing program used to generate the Petition.

/DEBORAH E. FISHMAN/
Deborah E. Fishman
Reg. No. 48,621

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§ 42.6(e) and 42.105(a) and (b), I certify that on the date listed below, a copy of this paper and every exhibit filed with this paper was served on the patent owner at the correspondence address of record and elsewhere, as listed below:

Knobbe Martens Olson & Bear LLP
2040 Main Street, 14th Floor
Irvine, CA 92614

Thomas W. Burns
Glaukos Corporation
229 Avenida Fabricante
San Clement, CA 92672

Dated: May 23, 2018

/DEBORAH E. FISHMAN/
Deborah E. Fishman
Reg. No. 48,621