



October 29, 2008

PMA Document Mail Center (HFZ-401)
Office of Device Evaluation
Center for Devices and Radiological Health
9200 Corporate Boulevard
Rockville, MD 20850

RE: P050034 – Amendment 16
VisionCare Ophthalmic Technologies Implantable Miniature Telescope
IMT (by Dr. Isaac Lipshitz)TM

Dear Sir or Madam,

Please find enclosed three (3) copies of Amendment 16 to P050034, for the Implantable Miniature Telescope (IMT).

This amendment provides responses to three information requests by the Division of Ophthalmic and ENT Devices (DOENTD). These requests for information were submitted via email to Gene Hilmantel, O.D., M.S. on October 27, 2008:

Item 1: Response to email dated October 16, 2008

Item 2: Response to email dated October 20, 2008

Each original email request is followed by VisionCare's response, with the requested information.

Thank you for your consideration of this PMA P050034 as amended. If you have any questions or need any additional information during your review, please contact me at (949) 715-0609 (phone), or by fax at (949) 715-0610, or by email at judy@clinregconsulting.com.

Sincerely,

Judy F. Gordon, D.V.M.
Regulatory Consultant to VisionCare Ophthalmic Technologies, Inc.



P050034
AMENDMENT 016
VISIONCARE OPHTHALMIC TECHNOLOGIES
IMPLANTABLE MINIATURE TELESCOPE™ (IMT BY DR. ISAAC LIPSHITZ)

OCTOBER 29, 2008

APPLICANT

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CORRESPONDENT

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P050034 AMENDMENT 016
VISIONCARE OPHTHALMIC TECHNOLOGIES
IMPLANTABLE MINIATURE TELESCOPE

ITEM 1. RESPONSE TO EMAIL DATED OCTOBER 16, 2008

ITEM 2. RESPONSE TO EMAIL DATED OCTOBER 20, 2008

RESPONSE TO EMAIL DATED OCTOBER 16, 2008

With regard to the late cases of corneal edema and the line listings provided in amendment 13, we have been unable to locate any information on how they were treated (hyperosmotics? And whether or not the late corneal edema has resolved in any way, the decompensation and transplant cases excepted. Could you please provide us with this information? For each eye, please include duration of the adverse event, treatment, sequelae, and investigator's evaluation of the relationship of the event to the device.

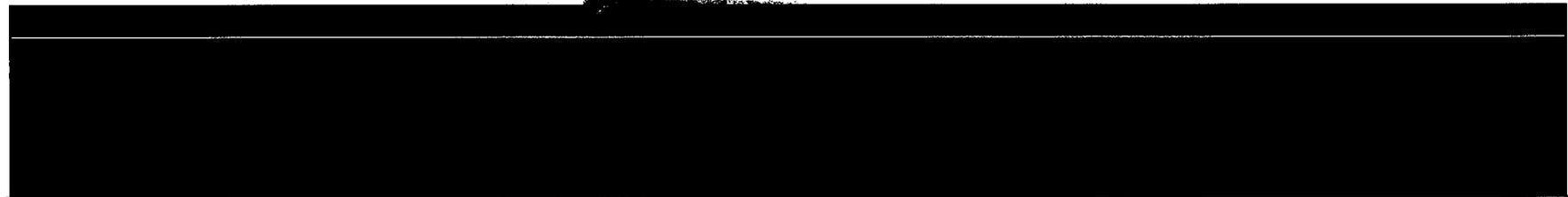
Response:

The previously submitted line listings on cases of corneal edema have been expanded to include the requested information. We have also included comments on each subject with late corneal edema previously included in various submissions, to facilitate review of the available information on these study subjects.

DATA LISTING FOR IMT-IMPLANTED EYES WITH CORNEAL EDEMA AT > 3 MONTHS

N = 12

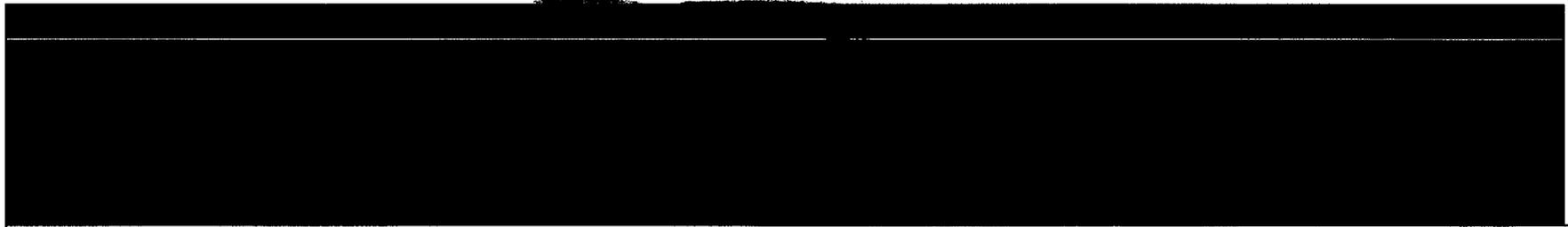
02/21/03	PREOP	-40	2642	59.7	35.3	546	Corneal edema reported on 08/08/06 (1224 days postop, 42 month visit)	None	Corneal edema unresolved	Not Related	None
06/20/03	3M	79				574					
08/26/03	6M	146	2274	52.0	36.3	561					
01/16/04	9M	289	2326	63.3	37.0	578					
03/19/04	12M	352	1855	49.3	36.0	569					
09/14/04	18M	531	1929	56.0	35.0	586					
03/08/05	24M	706	1011	58.7	32.3	597					
08/08/06	42M	1224	508	33.0	28.7						
03/06/07	48M	1434	660	61.0	25.3	656					
08/28/07	54M	1609	556	50.0	46.0	642					
02/26/08	ECD only (60 Months)	1791	505	33.0	17.5						
COMMENTS											
Transient corneal edema reported on Day 1.											



08/06/03	PREOP	-42	2908	59.0	31.0	607	Corneal edema reported on 05/15/06 (971 days postop, at 36-month visit)	Loteprednol	Corneal Decompensation 02/02/07 (1,234 days postop) Subject died of unknown case on 10/01/07	Possibly Related	None
12/12/03	3M	86	432	52.7	35.3	621					
03/16/04	6M	181	452	49.7	27.0	677					
05/18/04	9M	244	397	38.3	42.3	601					
08/24/04	12M	342	361	67.0	33.5	694					
01/11/05	18M	482	351	54.3	33.7	700					
05/10/05	24M	601				771					
05/15/06	36M	971									
02/02/07	42M	1234				771					
09/04/07	48M	1448				920					

COMMENTS:

For Subject [REDACTED], the study investigator documented operative trauma consisting of endothelial touch during implantation, with resulting early change in ECD, and early corneal edema (Day 1) as well as late corneal edema leading to corneal decompensation.



01/17/03	PREOP	-40				516	Corneal edema reported on 01/18/05 (687 days postop, 24 month visit)	Muro 128; Prednisolone acetate	Corneal Transplant 12/06/06 (1379 days postop)	Definitely related	<ul style="list-style-type: none"> ▪ ACD <3.0 mm ▪ Surgical order ≤ 5 ▪ Non-cornea specialist
01/23/03	ECD only (Preop)	-34	2763	67.3	28.0						
05/22/03	3M	85	1684	60.3	34.0	528					
08/12/03	6M	167	1380	51.7	32.3	508					
12/04/03	9M	281	1070	64.0	31.0	516					
02/12/04	12M	351	845	52.0	27.0	499					
06/10/04	18M	470	604	20.0	21.0	569					
01/08/05	ECD only (24 Months)	682	529	56.3	23.7						
01/18/05	24M	692				580					
03/20/07	48M	1483				550					
07/24/07	54M	1609				558					
02/26/08	60M	1826				602					

COMMENTS:

Subject [REDACTED] presented with ACD <3.0 mm, surgical order ≤5, and was operated by a non-cornea specialist, all risk factors for greater endothelial cell loss.

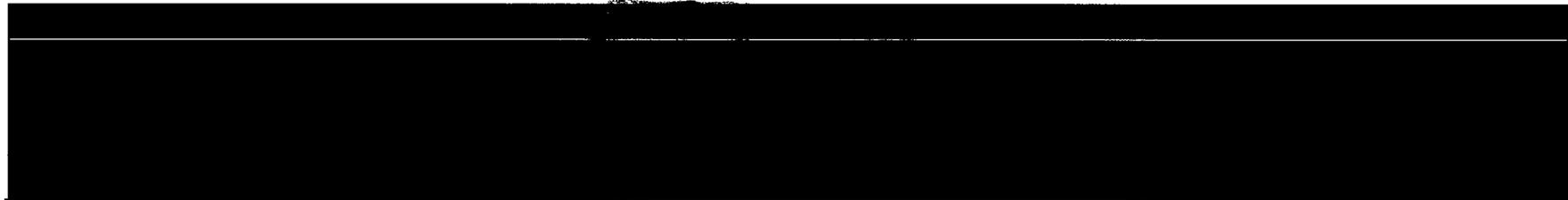
Iris damage and corneal touch were reported intraoperatively, with transient corneal edema at Day 1 and Day 7. BCVA improved following surgery through 12 months, but decreased over time as a result of corneal edema. ECD had decreased to 529 cells/mm² at 24 months. At approximately 48 months postoperatively, penetrating keratoplasty was performed, and the IMT was left in place. Post-keratoplasty, recovery was uneventful and visual acuity improved very significantly, from 20/800 to 20/160.

08/01/03	PREOP	-41	2860	57.3	33.7	610	Corneal edema reported on 04/09/04 (211 days postop)	Prednisolone acetate 1% q2h while awake for 1 week, QID for 1 week, TID for 1 week, BID for 3 days	None, corneal edema resolved	Probably Related	Corneal guttata
12/01/03	3M	81	2694	55.0	35.7	602					
02/02/04	6M	144	2737	60.3	32.0	607					
04/09/04	Interim	211				721					
05/03/04	9M	235				592					
05/04/04	ECD only (9 Months)	236	2816	54.3	35.7						
07/19/04	12M	312	2434	37.0	30.3	595					
11/06/06	36M	1152	2336	59.0	32.0	593	Resolution 05/03/04, at 9 month visit				
							Duration 24 days				

COMMENTS:

In Subject [REDACTED], corneal edema was observed between the 6-month and 9-month visits, and resolved completely, with no corneal edema was observed in this subject at 12 and 36 months. ECD remained high at 2336 cells/mm² at 36 months.

NB: Review of this case by a medical monitor suggests that corneal edema may be inflammatory in nature, or have an inflammatory component and can be managed by steroids, as evidenced by the good resolution of corneal edema in this eye.



06/30/03	PREOP	-11	2455	55.0	36.3	546	Corneal edema reported on 04/15/05 (644 days postop) Resolution 10/28/05 (interim visit) Duration 196 days	Muro 128 QID	Corneal edema reported to have resolved; however, CCT remains increased from baseline	Not related	<ul style="list-style-type: none"> ▪ ACD <3.0 mm ▪ Non-cornea specialist
10/10/03	3M	91	2211	54.3	35.0	542					
01/14/04	6M	187	1074	48.0	37.7	559					
04/05/04	9M	269	1048	48.3	32.7	567					
07/14/04	12M	369	955	62.0	29.7	633					
01/07/05	18M	546	553	45.0	26.3	662					
04/15/05	24M	644				716					
06/20/05	Interim	710	519	46.0	21.7	548					
08/21/06	36M	1137				658					
01/03/07	42M	1272	618	56.3	30.7	724					
06/11/07	48M	1431	719	40.0	30.0	633					

COMMENTS:

Subject [REDACTED] presented with ACD <3.0 mm and was operated by a non-cornea specialist, risk factors for greater endothelial cell loss. Early corneal edema was reported on Day 1.

08/29/03	PREOP	-24	1909	61.0	32.7	553	Corneal edema reported on 06/25/04 (277 days postop, at 9 month visit)	Muro 128 drops and ointment	Corneal Decompensation 06/25/05 (277 days)	Probably Related	<ul style="list-style-type: none"> ▪ ACD <3.0 mm ▪ Non-cornea specialist
01/14/04	3M	114	633	58.3	22.0	565					
04/27/04	6M	218	463	59.0	31.3	635					
06/25/04	9M	277				730					
08/17/04	12M	330				155					
09/09/04	Interim	353	3128	58.0	37.3	629					
10/07/04	Interim	381	3442	55.3	34.3	581					
01/18/05	Imterim	484	3133	50.3	42.0	549					
05/11/05	Interim	597	2984	51.3	35.3	546					

COMMENTS:

Subject ██████ presented with ACD <3.0 mm and was operated by a non-cornea specialist, both risk factors for greater endothelial cell loss.

In Subject ██████ during implantation of the IMT, spontaneous prolapse of the superior iris occurred, preventing visualization of the capsular bag. The IMT was placed in the ciliary sulcus, and at the end of the procedure, the IMT was in place with moderate depth of the anterior chamber. The superior iris was atrophic due to the prolapse and did not constrict with a miotic agent. On postoperative day 1, best corrected visual acuity was limited to hand motion; slit lamp examination revealed corneal edema, endothelial folds, and anterior chamber cells and flare, and anterior synechiae. Intraocular pressure was 22 mmHg. The anterior chamber was deep and the IMT was centered. Anterior synechiae persisted through the course of follow-up.

At the 7 day visit, the corneal incision was secure, and Seidel negative, with IOP of 18 mmHg. The anterior chamber was shallow with the IMT surface close to the corneal endothelium. However, the subject was not using a protective shield at all times and was not limiting activity, as instructed by the study investigator.

At the 6 month visit, visual acuity had improved by 4.6 lines. Slit lamp examination revealed normal cornea, 1+ folds, no cells and no flare in the anterior chamber. Endothelial cell density had further decreased to 463.3 cells/mm.² Intraocular pressure was 14 mmHg. The IMT was centered and on close inspection, there was a subtle area of Descemet's fold.

At the 9 month visit, best corrected visual acuity was 20/300, and intraocular pressure was 14 mmHg. The anterior chamber was deep and the IMT was centered. The superior iris was updrawn. Centrally, the cornea had 2+ endothelial folds. A diagnosis of corneal decompensation was made by the study investigator, most likely attributable to endothelial touch during the first postoperative week when the subject as not wearing a shield and not limiting his activity, despite instructions to the contrary. Treatment with Muro 128 was initiated, and the subject underwent corneal transplantation September 1, 2004; the IMT was removed and a MA60 22.0 diopter lens was implanted in the ciliary sulcus.

The postoperative follow-up for this subject was uneventful. The subject was evaluated for 6 months following the transplant, and there were no sequelae of the corneal transplant procedure.

*Post transplant ECD excluded from primary ECD analyses

06/05/03	PREOP	-39	2465	66.0	29.7	551	Corneal edema reported on 06/28/07 (1,145 days postop, at interim visit)	None	Corneal Decompensation 10/24/07 (1,563 days) Subject died of lung cancer on 06/27/08	Probably Related	<ul style="list-style-type: none"> ▪ ACD <3.0 mm ▪ Surgical order ≤ 5 ▪ Non-cornea specialist
10/14/03	3M	92				590					
10/27/03	ECD only (3 Months)	105	782	57.0	25.3						
02/03/04	6M	204	431	42.7	28.0	626					
04/27/04	9M	288	309	50.0	14.7	708					
07/14/04	12M	366	311	39.0	26.0	736					
12/15/04	18M	520	664	26.0	33.3	641					
04/19/05	ECD only (24 Months)	645	503	49.0	28.0						
04/20/05	24M	646				611					
09/19/06	36M	1163	823	61.3	41.3						
02/14/07	42M	1311	594	58.0	20.0	706					
06/12/07	48M	1429	501	25.0	37.0	741					

COMMENTS:

Subject [REDACTED] presented with ACD <3.0 mm, surgical order ≤5, and was operated by a non-cornea specialist, all risk factors for greater endothelial cell loss.

09/26/03	PREOP	-24				565	Corneal edema reported on 10/25/06 (1,101 days postop, at 36 month visit)	Muro 128 Pilocarpine	Corneal Transplant, IMT left in eye 08/15/07 (1,395 days)	Definitely Related	<ul style="list-style-type: none"> ▪ Guttata ▪ Surgical order <5 cases
10/06/03	ECD only (Preop ECD)	-14	2774	58.0	40.0						
01/07/04	3M	79				585					
04/27/04	6M	190	2566	45.0	28.5	590					
06/09/04	9M	233	2814	57.3	42.7	596					
08/25/04	12M	310	2959	51.0	45.3	599					
02/08/05	ECD only (18 Months)	477	2748	51.0	41.3						
02/09/05	18M	478				605					
06/07/05	ECD only (24 Months)	596	2860	58.7	39.7						
06/08/05	24M	597				640					
10/25/06	36M	1101	2444	53.3	39.0						
12/04/06	CCT only (36 Months)	1141				655					
05/07/07	42M	1295	841	53.3	34.7	770					
10/25/07	48M	1466	2153	58.3	32.0	534					
04/22/08	ECD only (54 Months)	1646	1405	53.0	32.0						

COMMENTS

In Subject [REDACTED] the IMT was successfully implanted, however the device was tilted, such that the superior haptic pressed against the temporal iris. In this eye, only relatively modest decreases in ECD were observed through 36 months of follow-up, when the subject presented with localized corneal edema, in the inferotemporal cornea corresponding to intermittent touch of the IMT to the endothelium. The position of the IMT was initially managed with the use of 1% pilocarpine, however, proper positioning of the IMT was achieved only intermittently. Although the study medical monitor and the sponsor communicated to the study investigator that IMT repositioning was not advisable, repositioning of the IMT was attempted. This procedure induced further trauma to the endothelium with corneal touch.

Following this attempt at repositioning the IMT, there was further deterioration of the cornea, with corneal edema and loss of visual acuity. Corneal transplantation was performed approximately 48 months following original placement of the IMT, and the device was left in place. Recovery was uneventful, with a clear graft and good visual rehabilitation.

04/30/03	PREOP	-35	2738	62.0	31.7	557	Corneal edema reported on 03/09/05 (644 days postop, at 24 month visit) Duration 861 days (was resolved at 48 month visit)	Muro 128 QID, Prednisolone Acetate QID	None, corneal edema resolved	Probably Related	<ul style="list-style-type: none"> ▪ ACD <3.0 mm ▪ Surgical order ≤ 5 ▪ Non-cornea specialist
08/12/03	3M	69	1315	57.7	34.7	519					
12/18/03	6M	197	846	68.7	30.0	619					
03/10/04	9M	280	656	46.0	23.3	646					
06/30/04	12M	392	446	64.3	30.7	604					
12/08/04	Interim	553	628	60.0	25.0	645					
03/09/05	24M	644	676	50.0	14.0	715					
09/20/06	42M	1204	983	56.7	44.0						
07/18/07	48M	1505	851	48.3	32.3	598					

COMMENTS:

Subject [REDACTED] had an anterior chamber depth of <3.0 mm, was an early surgical case (surgical order ≤5), and the surgery was performed by a non-cornea specialist, all risk factors for greater endothelial cell loss.

NB: Review of this case by a medical monitor suggests that corneal edema may be inflammatory in nature, or have an inflammatory component and can be managed by steroids, as evidenced by the good resolution of corneal edema in this eye.

07/15/03	PREOP	-76				599	Corneal edema reported on 04/17/08 (1,662 days postop, at 54-month visit)	None	Corneal edema unresolved	Definitely Related	<ul style="list-style-type: none"> ▪ ACD <3.0 mm ▪ Non-cornea specialist
08/26/03	ECD only (Preop ECD)	-34	2463	66.3	29.7						
01/21/04	3M	114	1901	59.0	27.3	536					
03/23/04	6M	176	1554	55.3	31.0	559					
05/11/04	9M	225	1170	59.0	32.0	658					
08/19/04	12M	325	901	70.7	22.3	588					
01/28/05	18M	487	638	56.0	22.3	534					
05/10/05	24M	589	544	57.3	25.0	640					
08/14/06	36M	1050	386	55.7	30.3						
02/19/07	42M	1239	393	50.0	9.5	553					
08/27/07	48M	1428				612					
04/17/08	54M	Only an adverse event form has been submitted, reporting corneal edema									

COMMENTS:

Intraoperatively, Subject [REDACTED] had extensive complications, including posterior capsule rupture and vitreous loss requiring vitrectomy. This subject had a shallow anterior chamber (<3.0 mm) at baseline, as well as surgery performed by a non-cornea specialist, both risk factors for greater endothelial cell loss.

Vitreous was observed in the anterior chamber on Day 7, and was still present at 1 month. At the 1 month visit, iris atrophy and transillumination defects were reported, and both of these findings persisted through the available follow-up for this subject.

09/25/03	PREOP	-34	1769	67.0	27.7	600	Corneal edema reported on 09/06/06 (1,043 days postop, 36 month visit)	Corneal edema not resolved	Definitely Related	<ul style="list-style-type: none"> ▪ ACD <3.0 mm ▪ Non-cornea specialist
01/07/04	3M	70	916	55.7	31.7	576				
04/29/04	6M	183	646	67.0	24.0	705				
07/08/04	9M	253	531	67.0	19.7	433				
09/14/04	12M	321	519	53.3	28.0	570				
02/01/05	18M	461	457	60.7	29.7	589				
06/14/05	24M	594	505	51.3	37.0	631				
09/06/06	36M	1043	324							
04/18/07	42M	1267	709	47.0	32.0	712				
COMMENTS:										
Subject [REDACTED] had a shallow anterior chamber (<3.0 mm) at baseline and were operated by non-cornea specialists, both risk factors for greater endothelial cell loss.										

08/20/03	PREOP	-48	2118	61.3	31.3	607	Corneal edema reported on 12/18/03 (72 days postop, 3 month visit)	None	Corneal decompensation 06/17/04 (254 days) Corneal transplant 08/10/04 (308 days)	Definitely Related	<ul style="list-style-type: none"> ▪ ACD <3.0 mm ▪ Surgical order ≤ 5
12/18/03	3M	72				706					
03/04/04	6M	149	385	46.0	30.5	742					
08/05/04	12M	303				955					
10/16/06	36M	1105				641					
04/03/07	42M*	1274	1857	60.3	35.3	622					
10/25/07	48M	1479				622					

COMMENTS:

In Subject [REDACTED], intraoperative positive vitreous pressure resulted in iris prolapse. On the first postoperative day, intraocular pressure was increased and the inferior aspect of the IMT was covered by the inferior iris. Iris atrophy was reported as a complication at Day 1, and corneal edema was observed at Day 1 (3+) and Day 7 (2+), resolving to 1+ at 1, 3 and 6 months. (NB: Since the corneal edema was still present at 3 and 6 months, this has been reported in the category of corneal edema present at >3 months). Corneal edema progressed at 9 months. Over the course of follow-up, the IMT was observed to be decentered inferiorly, with one of the haptics in the sulcus rather than in the capsular bag.

Starting approximately 4 months postoperatively, the subject started to experience poor vision, and visual acuity decreased to count fingers. The IMT was still slightly decentered inferiorly, but stable without any marked decentration or tilting. Over the next several months, the subject's visual acuity gradually deteriorated and corneal edema worsened. Treatment with topical prednisolone acetate 1% was increased, and Muro 128 (drops and ointment) was added to the therapeutic regimen. At 6 months, endothelial cell density had decreased to 385.3 cells/mm² and the corneal edema continued to progress. On this basis a decision was made to perform a corneal transplantation.

The subject underwent corneal transplantation on August 10, 2004. During corneal transplantation, the surgeon attempted to reposition the IMT, however, when the surgeon tried to move the haptic from the sulcus, the posterior capsule ruptured. Subsequently an anterior chamber IOL was inserted.

The postoperative period was uneventful. At three subsequent examinations on November 22, 2004, December 16, 2004 and February 23, 2005, slit lamp examinations revealed normal cornea, no endothelial folds, with no cells and no flare in the anterior chamber. Intraocular pressure was varied from 12 to 22 mmHg. No complications or adverse events were reported.

*Post transplant ECD excluded from primary ECD analyses

RESPONSE TO OCTOBER 20, 2008 EMAIL

- 1. Please clarify the following concerning the comparability of the initial 2-year IDE study (Protocol IMT-002) and the continuation study (IMT-002-LTM):**

I. What number of eyes and percentage of implanted eyes had:

- A. ECD of <1000 at any visit at Month 24 or prior**
- B. ECD of <1500 at any visit at Month 24 or prior**
- C. Had a within-eye average (months 6-24) ECD <1000. (This has been previously provided.)**
- D. Had a within-eye average (months 6-24) of ECD <1500.**

Include the subject numbers for all categories.

II. For these four groups, what percent (and number of eyes) continued in the continuation study?

Response:

The number and percentage of eyes with ECD <750 cells/mm², <1000 cells/mm², and <1500 cells/mm² are presented in Tables 1 through 3 on the following pages. Within-eye differences in ECD (months 6-24) are presented in Table 4 through 6.

Additionally, as shown in the attached tables, the majority of patients continued in the continuation study, i.e., IMT-002-LTM.

As shown in these tables, all but 6 of the eyes with ECD loss < 750, <1000 and <1500 cells/mm² presented with at least one of the risk factors for greater endothelial cell loss, i.e., ACD less than 3.0 mm, guttata, surgery performed by non-corneal specialists, and surgery among the first 5 cases of the study surgeon. The majority of eyes had multiple risk factors for ECD loss.

TABLE 1
ECD < 750 CELLS/MM² BEFORE OR AT 24 MONTHS
IMT-IMPLANTED EYES

Page 1 of 1

n/N (%)	0/206 (0%)	6/193 (3%)	8/198 (4%)	9/190 (5%)	9/186 (5%)	13/180 (7%)	12/171 (7%)	
Mean	2334	1023	849	783	714	649	651	
*	2908	432	452	397	361	351		
*	2763	1684	1380	1070	845	604	529	2, 3, 4
	2709	583						2, 4
	2009	754	890	698	791	813	825	1, 4
*	1739		925	1051	858	901	730	2, 3
	1821	1606	1673	1297	1214	736		4
*	2455	2211	1074	1048	955	553	519	2, 4
*	1768	949	876	699	747	754	672	3, 4
*	1909	633	463					2, 4
	2225	679	753	608	504	434	436	3, 4
*	3012	755	884	865	1000	698	1000	3, 4
*	2465	782	431	309	311	664	503	2, 3, 4
*	2598	1187	615	568	592	639	615	3, 4
*	1862	492	488	515	478	489	386	1, 2, 3, 4
*	2738	1315	846	656	446	628	676	2, 3, 4
*	2463	1901	1554	1170	901	638	544	2, 4
*	1769	916	646	531	519	457	505	2, 4
*	2889	808	1083	821	742	659	735	1, 3, 4
*	2457	733	713	1011	874	1009	1088	2, 3, 4
*	2118		385					2, 3
16/20 (80%)								

ECD after IMT explant was excluded.

Risk Factors: 1: guttata, 2: ACD < 3.0 mm, 3: Surgical Order 1 to 5, 4: Non-Cornea Specialist

IMT-002 minimum ECD exclusion criteria – ECD < 1600 cells/mm²

*Continuing to IMT-002-LTM Study.

TABLE 2
ECD < 1000 CELLS/MM² BEFORE OR AT 24 MONTHS
IMT-IMPLANTED EYES

N/N (%)	0/206 (0%)	16/193 (8%)	17/198 (9%)	16/190 (8%)	21/186 (11%)	21/180 (12%)	19/171 (11%)	
MEAN	2335	1057	952	871	795	765	771	
*	2908	432	452	397	361	351		
*	2763	1684	1380	1070	845	604	529	2, 3, 4
	2424	966	1105	890				2, 3, 4
*	2477	1072	1320	1309	957	1328	1117	3, 4
	2709	583						2, 4
*	2160	1625	983	1582	997	1546	1234	1, 4
*	2532	803	793	782	789	785	831	1, 2, 3, 4
*	2487	909			1278	952	982	3, 4
	2009	754	890	698	791	813	825	1, 4
	2065	1307	1554	971		804	1294	3
*	1739		925	1051	858	901	730	2, 3
	1853	911	888	792	877	782	772	3, 4
	1821	1606	1673	1297	1214	736		4
*	2455	2211	1074	1048	955	553	519	2, 4
*	1768	949	876	699	747	754	672	3, 4
*	1909	633	463					2, 4
*	2812	1280	1533	1241	1091	1077	956	1, 2, 3, 4
	2225	679	753	608	504	434	436	3, 4
*	3012	755	884	865	1000	698	1000	3, 4
*	2465	782	431	309	311	664	503	2, 3, 4
*	2598	1187	615	568	592	639	615	3, 4
*	1862	492	488	515	478	489	386	1, 2, 3, 4
	2234	1235	1385	905	960	813	796	3, 4
*	2738	1315	846	656	446	628	676	2, 3, 4
*	2463	1901	1554	1170	901	638	544	2, 4
*	1769	916	646	531	519	457	505	2, 4
*	2889	808	1083	821	742	659	735	1, 3, 4
*	2457	733	713	1011	874	1009	1088	2, 3, 4
*	2118		385					2, 3
21/29 (72%)								

ECD after IMT explant was excluded.

Risk Factors: 1: guttata, 2: ACD < 3.0 mm, 3: Surgical Order 1 to 5, 4: Non-Cornea Specialist
 IMT-002 minimum ECD exclusion criteria – ECD < 1600 cells/mm²

* Continuing to IMT-002-LTM Study.

TABLE 3
ECD < 1500 CELLS/MM² BEFORE OR AT 24 MONTHS
IMT-IMPLANTED EYES

N/N (%)	0/206 (0%)	33/193 (17%)	41/198 (21%)	42/190 (22%)	44/186 (24%)	46/180 (26%)	45/171 (26%)	
MEAN	2329	1375	1322	1288	1206	1188	1161	
*	2642		2274	2326	1855	1929	1011	
*	2967		2644	2246	1028	2689	2184	
*	2908	432	452	397	361	351		
*	2480	1673	1887	1730	1406	1499	1285	2
*	2038	1576	1452	1405	1400	1439	1351	
*	1695	1591	1501	1441	1639	1437	1522	2
*	2763	1684	1380	1070	845	604	529	2, 3, 4
	2424	966	1105	890				2, 3, 4
*	2477	1072	1320	1309	957	1328	1117	3, 4
*	2376	1117	1241	1220	1173	1108	1134	2, 3, 4
	3305	1862	1369	1708	1617	1765	1620	4
	2709	583						2, 4
*	2160	1625	983	1582	997	1546	1234	1, 4
*	1975	1508	1493	1520	1487	1500	1473	2, 4
	2483	1415	1428	1368	1346	1425	1447	3, 4
*	2532	803	793	782	789	785	831	1, 2, 3, 4
	2253	1917	1577	1724	1433	1399	1597	2, 3, 4
*	2071	1639	1488	1473	1400	1476	1461	4
*	2487	909			1278	952	982	3, 4
	2209	1590	1506	1435				2, 4
	2009	754	890	698	791	813	825	1, 4
	2065	1307	1554	971		804	1294	3
*	1739		925	1051	858	901	730	2, 3
	1853	911	888	792	877	782	772	3, 4
*	2234	1207	1503	1579	1623	1691	1525	4
	1821	1606	1673	1297	1214	736		4
*	2416	1876	1787	1431	1279	1226	1089	2, 4
*	2455	2211	1074	1048	955	553	519	2, 4
*	1768	949	876	699	747	754	672	3, 4
	2058	2033	1812	1803	1565	1390	1473	3, 4
*	1909	633	463					2, 4
	2134	1795	1495	2122	1402	1451	1365	3
*	1723	1636	1593	1399	1276	1351	1049	2
*	2641	1186	1598	1739	1524	1704	1589	
*	2812	1280	1533	1241	1091	1077	956	1, 2, 3, 4
*	1871	1804	1842	1525	1521	1222	1312	1, 3, 4
	2225	679	753	608	504	434	436	3, 4

*	2968	1497	1237	1423	1388	1379	1424	2, 3, 4
	3012	755	884	865	1000	698	1000	3, 4
	2087	1861	2029	1525	1530	1373	1365	3, 4
*	2357	1572	1832	1609	1416	1990	1367	2, 4
*	2861	1357	1038	1409	1612	1335	1541	3, 4
	2465	782	431	309	311	664	503	2, 3, 4
*	2598	1187	615	568	592	639	615	3, 4
*	1862	492	488	515	478	489	386	1, 2, 3, 4
	2385	2020	1972	1327	2108	1312	1149	3, 4
	2429	1322	1274		1325			2, 3, 4
*	2254	1821	1395	1818	1665	1901	1659	2, 3, 4
*	2416	1323	2045	1500	1531	1154	1084	1, 4
	2234	1235	1385	905	960	813	796	3, 4
	2529	1334	1251	1234				2, 4
	2263	1634	1322	1429	1507		1599	3
*	1816	1370	1387	1008	1144	1034	1194	1, 3
*	2738	1315	846	656	446	628	676	2, 3, 4
*	2463	1901	1554	1170	901	638	544	2, 4
*	1769	916	646	531	519	457	505	2, 4
*	2835	2105	1380	1850	1967	2218	2193	3, 4
*	2642	1868	1440	1457	1407	1425	1467	3, 4
*	2889	808	1083	821	742	659	735	1, 3, 4
	2290	1593	1600	1478	1679		1583	3, 4
*	2771	1886	1816	1722	1368	1336	1223	3, 4
*	2457	733	713	1011	874	1009	1088	2, 3, 4
	1875	1227	1238	1447	1411			1, 4
*	2001	1536	1513	1536	1471	1421	1354	2, 3, 4
	1916	1720	1380	1619	1172	1463	1194	1, 2, 3, 4
*	2042	1634	1616	1499	1616	1581	1577	2, 3, 4
*	2118		385					2, 3

45/67 (67%)

ECD after IMT explant was excluded.

Risk Factors: 1: guttata, 2: ACD < 3.0 mm, 3: Surgical Order 1 to 5, 4: Non-Cornea Specialist
 IMT-002 minimum ECD exclusion criteria – ECD < 1600 cells/mm²

* Continuing to IMT-002-LTM Study.

TABLE 4
INTRA-EYE ECD AVERAGE (6 TO 24 MONTHS) < 750 CELLS/MM²
IMT-IMPLANTED EYES

MEAN	2236	821	596	535	494	552	542	
	2908	432	452	397	361	351		
*	1768	949	876	699	747	754	672	3, 4
*	1909	633	463					2, 4
	2225	679	753	608	504	434	436	3, 4
*	2465	782	431	309	311	664	503	2, 3, 4
*	2598	1187	615	568	592	639	615	3, 4
*	1862	492	488	515	478	489	386	1, 2, 3, 4
*	2738	1315	846	656	446	628	676	2, 3, 4
*	1769	916	646	531	519	457	505	2, 4
*	2118		385					2, 3
9/10 (90%)								

ECD after IMT explant was excluded.

Risk Factors: 1: guttata, 2: ACD < 3.0 mm, 3: Surgical Order 1 to 5, 4: Non-Cornea Specialist
 IMT-002 minimum ECD exclusion criteria – ECD < 1600 cells/mm²

* Continuing to IMT-002-LTM Study.

TABLE 5
INTRA-EYE ECD AVERAGE (6 TO 24 MONTHS) < 1000 CELLS/MM²
IMT-IMPLANTED EYES

MEAN	2327	1007	847	769	713	667	676	
	2908	432	452	397	361	351		
*	2763	1684	1380	1070	845	604	529	2, 3, 4
	2424	966	1105	890				2, 3, 4
*	2532	803	793	782	789	785	831	1, 2, 3, 4
	2009	754	890	698	791	813	825	1, 4
*	1739		925	1051	858	901	730	2, 3
	1853	911	888	792	877	782	772	3, 4
*	2455	2211	1074	1048	955	553	519	2, 4
*	1768	949	876	699	747	754	672	3, 4
*	1909	633	463					2, 4
	2225	679	753	608	504	434	436	3, 4
*	3012	755	884	865	1000	698	1000	3, 4
*	2465	782	431	309	311	664	503	2, 3, 4
*	2598	1187	615	568	592	639	615	3, 4
*	1862	492	488	515	478	489	386	1, 2, 3, 4
	2234	1235	1385	905	960	813	796	3, 4
*	2738	1315	846	656	446	628	676	2, 3, 4
*	2463	1901	1554	1170	901	638	544	2, 4
*	1769	916	646	531	519	457	505	2, 4
*	2889	808	1083	821	742	659	735	1, 3, 4
*	2457	733	713	1011	874	1009	1088	2, 3, 4
*	2118		385					2, 3
17/22 (77%)								

ECD after IMT explant was excluded.

Risk Factors: 1: guttata, 2: ACD < 3.0 mm, 3: Surgical Order 1 to 5, 4: Non-Cornea Specialist
 IMT-002 minimum ECD exclusion criteria – ECD < 1600 cells/mm²

* Continuing to IMT-002-LTM Study.

TABLE 6
INTRA-EYE ECD AVERAGE (6 TO 24 MONTHS) < 1500 CELLS/MM²
IMT-IMPLANTED EYES

MEAN	2299	1280	1176	1119	1054	986	1003	
* 2908	432	452	397	361	351			
* 2038	1576	1452	1405	1400	1439	1351		
* 2763	1684	1380	1070	845	604	529		2, 3, 4
	2424	966	1105	890				2, 3, 4
* 2477	1072	1320	1309	957	1328	1117		3, 4
* 2376	1117	1241	1220	1173	1108	1134		2, 3, 4
* 2160	1625	983	1582	997	1546	1234		1, 4
* 1975	1508	1493	1520	1487	1500	1473		2, 4
	2483	1415	1428	1368	1346	1425	1447	3, 4
* 2532	803	793	782	789	785	831		1, 2, 3, 4
* 2071	1639	1488	1473	1400	1476	1461		4
* 2487	909			1278	952	982		3, 4
	2209	1590	1506	1435				2, 4
	2009	754	890	698	791	813	825	1, 4
	2065	1307	1554	971		804	1294	3
* 1739		925	1051	858	901	730		2, 3
	1853	911	888	792	877	782	772	3, 4
	1821	1606	1673	1297	1214	736		4
* 2416	1876	1787	1431	1279	1226	1089		2, 4
* 2455	2211	1074	1048	955	553	519		2, 4
* 1768	949	876	699	747	754	672		3, 4
* 1909	633	463						2, 4
* 1723	1636	1593	1399	1276	1351	1049		2
* 2812	1280	1533	1241	1091	1077	956		1, 2, 3, 4
* 1871	1804	1842	1525	1521	1222	1312		1, 3, 4
	2225	679	753	608	504	434	436	3, 4
* 2968	1497	1237	1423	1388	1379	1424		2, 3, 4
* 3012	755	884	865	1000	698	1000		3, 4
* 2861	1357	1038	1409	1612	1335	1541		3, 4
* 2465	782	431	309	311	664	503		2, 3, 4
* 2598	1187	615	568	592	639	615		3, 4
* 1862	492	488	515	478	489	386		1, 2, 3, 4
	2429	1322	1274		1325			2, 3, 4
* 2416	1323	2045	1500	1531	1154	1084		1, 4
	2234	1235	1385	905	960	813	796	3, 4
	2529	1334	1251	1234				2, 4
	2263	1634	1322	1429	1507		1599	3
* 1816	1370	1387	1008	1144	1034	1194		1, 3
* 2738	1315	846	656	446	628	676		2, 3, 4

2. What percentage of eyes at month 36 and month 48 had ECD <1000? <1500? (Include subject numbers)

Response:

The percentages of eyes with ECD <750, <1000, and <1500 cells/mm² at 36 and 48 months are shown in Tables 7 through 9.

Consistent with the eyes with these levels of ECD loss at or prior to 24 months, only 3 eyes presented with no risk factors for greater endothelial cell loss.

**TABLE 7
ECD < 750 CELLS/MM² AT 36 OR 48 MONTHS
IMT-IMPLANTED EYES**

N/N (%)	3/70 (4%)	7/88 (8%)	
MEAN	621	623	
		660	
		719	2, 4
	809	669	3, 4
	823	501	2, 3, 4
	517	668	3, 4
		427	1, 2, 3, 4
	386		2, 4
	324		2, 4
	866	718	3, 4

Excluding records after IMT explant
 IMT-002 minimum ECD exclusion
 criteria – ECD < 1600 cells/mm²
 Risk Factors - 1: guttata, 2: ACD < 3.0 mm,
 3: Surgical Order 1 to 5, 4: Non-Cornea
 Specialist

*	2463	1901	1554	1170	901	638	544	2, 4
*	1769	916	646	531	519	457	505	2, 4
*	2642	1868	1440	1457	1407	1425	1467	3, 4
*	2889	808	1083	821	742	659	735	1, 3, 4
*	2771	1886	1816	1722	1368	1336	1223	3, 4
*	2457	733	713	1011	874	1009	1088	2, 3, 4
	1875	1227	1238	1447	1411			1, 4
*	2001	1536	1513	1536	1471	1421	1354	2, 3, 4
	1916	1720	1380	1619	1172	1463	1194	1, 2, 3, 4
*	2118		385					2, 3
35/49 (71%)								

ECD after IMT explant was excluded.

Risk Factors — 1: guttata, 2: ACD < 3.0 mm, 3: Surgical Order 1 to 5, 4: Non-Cornea Specialist

IMT-002 minimum ECD exclusion criteria – ECD < 1600 cells/mm²

* Continuing to IMT-002-LTM Study.

TABLE 8
ECD < 1000 CELLS/MM² AT 36 OR 48 MONTHS
IMT-IMPLANTED EYES

N/N (%)	8/70 (11%)	15/88 (17%)	
MEAN	795	802	
	660		
	957	1, 4	
	880	1, 2, 3, 4	
	800	2, 4	
	719	2, 4	
	809	669	3, 4
	1192	972	4
		921	1, 2, 3, 4
	1075	901	1, 3, 4
		863	3, 4
	998	1009	2, 3, 4
	823	501	2, 3, 4
	517	668	3, 4
		427	1, 2, 3, 4
		851	2, 3, 4
	386		2, 4
	324		2, 4
	866	718	3, 4
	962	1113	2, 3, 4

Excluding records after IMT explant
 IMT-002 minimum ECD exclusion
 criteria – ECD < 1600 cells/mm²
 Risk Factors - 1: guttata, 2: ACD < 3.0 mm,
 3: Surgical Order 1 to 5, 4: Non-Cornea
 Specialist

TABLE 9
ECD < 1500 CELLS/MM² AT 36 OR 48 MONTHS
IMT-IMPLANTED EYES

N/N (%)	26/70 (37%)	37/88 (42%)	
MEAN	1150	1079	
		660	
1357			
1209	1356		2
1180	1276		
1401	1424		2
	1117		2, 3, 4
	957		1, 4
1421			2, 4
	880		1, 2, 3, 4
	1335		4
	1011		3, 4
1171			2, 3
	1439		4
	800		2, 4
	719		2, 4
809	669		3, 4
1192	972		4
1344	1384		3, 4
	1100		2
	921		1, 2, 3, 4
1075	901		1, 3, 4
	1377		2, 3, 4
	863		3, 4
998	1009		2, 3, 4
1355	1463		2, 3, 4
1488	1285		4
1274			2, 4
	1262		3, 4
823	501		2, 3, 4
517	668		3, 4
	427		1, 2, 3, 4
1077			1, 4
1206	1166		2, 3, 4
1335	1429		2, 4
1023			4
	1105		1, 3
	851		2, 3, 4

	1395	1066	1, 2, 4
	386		2, 4
	1619	1436	4
	324		2, 4
	1571	1441	3, 4
	866	718	3, 4
	962	1113	2, 3, 4
	1444	1564	2, 3, 4
	1516	1319	2, 3, 4

Excluding records after IMT explant
 IMT-002 minimum ECD exclusion criteria – ECD < 1600
 cells/mm²
 Risk Factors - 1: guttata, 2: ACD < 3.0 mm, 3: Surgical
 Order 1 to 5, 4: Non-Cornea Specialist

3. *Please clarify whether you have received any information concerning cases of corneal edema, explants or other significant adverse events in patients who were not re-consented into the continuation study.*

RESPONSE:

VisionCare has not received information on cases of corneal edema, explants or other significant adverse events for patients who were not re-consented into the IMT-002-LTM study.