

**Discussion Points for Expansion of the “Checklist of Information Usually Submitted in an Investigational Device Exemption (IDE) Application for Refractive Surgery Lasers” Draft Document**

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Diagnostic and Surgical Devices Branch  
Division of Ophthalmic Devices  
Office of Device Evaluation

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Comments and suggestions regarding this draft document should be submitted within 30 days of the above release date to Morris Waxler, Ph.D., Division of Ophthalmic Devices, 9200 Corporate Boulevard (HFZ 460), Rockville, MD 20850. Comments and suggestions received after this date may not be acted upon by the Agency until the document is next revised or updated. For questions regarding this draft document, contact Morris Waxler, Ph.D. at 301-594-2018.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Food and Drug Administration  
Center for Devices and Radiological Health

The following proposed revisions in Food and Drug Administration (FDA) guidance on refractive surgery lasers will be discussed at a public hearing on October 21, 1997. The objective is to extend this guidance to high myopia, astigmatism, and hyperopia based on current scientific and clinical knowledge. Other modifications also are proposed.

## **HIGH MYOPIA AND HYPEROPIA WITH AND WITHOUT ASTIGMATISM**

The proposed inclusion and exclusion criteria for study of the “normal” population as well as safety and effectiveness target values are summarized in the tables below.

### **PROPOSED MODIFICATIONS TO THE CURRENT LOW TO MODERATE MYOPIA GUIDANCE DOCUMENT**

- A. In Section 3.2.4.1. , change from “Contact lens wearers should:
1. remove soft or gas permeable contact lenses two weeks prior to baseline measurements
  2. remove hard contact lenses three weeks prior to baseline measurements, and have two central keratometry readings and two manifest refractions taken at least one week apart that do not differ by more than 0.50 diopter in either meridian; mires should be regular.”

To: “Contact lens wearers should remove soft or gas permeable contact lenses at least three days prior to baseline measurements. At that exam cycloplegic and manifest refractions as well as corneal topography should be obtained on both eyes. If the investigator determines that the topography is within normal limits, surgery may be scheduled at least one week after the initial exam, with no contact lens wear permitted prior to the surgery. If, on the day of scheduled surgery for the primary eye, central keratometry readings and manifest refraction spherical equivalents do not differ significantly from the initial exam measurements (by more than 0.50 diopter for low to moderate myopia and hyperopia, or by more than 1.0 diopter for high myopia), surgery can proceed. If the refractive change exceeds this criterion, the surgery should be rescheduled after refractive stability is achieved.

For fellow eyes, contact lens wear is permitted until at least three days prior to surgery. If, on the day of scheduled surgery for the fellow eye, central keratometry readings and manifest refraction spherical equivalents do not differ significantly from the initial exam measurements (by more than 0.50 diopter for low to moderate myopia and hyperopia, or by more than 1.0 diopter for high myopia), surgery can proceed. If the refractive change exceeds this criterion, the surgery should be rescheduled after refractive stability is achieved.”

- B. In Section 3.2.4., add the following language: “If there are scientific reasons for expecting different safety and effectiveness results based on gender or race, these demographic variables should be studied.”
- C. In Section 3.2.4.2., change “History of glaucoma or an intraocular pressure > 21 mm of Hg.” To: “History of glaucoma or glaucoma suspect.”
- D. In Section 3.2.1., delete “Haze beyond 6 months with loss of greater than 2 lines of BSCVA should occur in less than 1.0% of subjects”
- E. In Section 3.2.1., change “Measurement of endothelial cell loss is not necessary as long as laser refractive surgery is 250microns from the corneal endothelium and the laser parameters (e.g., wavelength and fluence) used are unlikely to damage the endothelium from this distance.” To: “Endothelial cell loss is an additional safety endpoint that needs to be evaluated when laser refractive surgery is performed closer than 200 microns from the corneal endothelium or the laser parameters (e.g., wavelength and fluence) used are likely to damage the endothelium.”
- F. Change the Examination Schedule Table from the one in Appendix A to the revised table below.
- G. In Section 3.2.6.1., change  
 “ E. Epithelium in the interface (LASIK only)  
 F. Lost, misplaced or misaligned flap (LASIK only)  
 G. Melting of the flap (LASIK only)  
 H. Uncontrolled IOP with increase of >5.0 mm HG above baseline, and any reading above 25.0 mm Hg”  
 To: “E. Epithelium in the interface with loss of 2 lines (10 letters) or more BSCVA (LASIK only)  
 F. Miscreated flap (lost, incomplete, too thin, ) (LASIK only)  
 G. Melting of the flap (LASIK only)  
 H. Uncontrolled IOP with increase of >10 mm HG above baseline, and any reading above 25 mm Hg”
- H. In Section 3.2.6.2., change  
 “H. Flap is not of the size and shape as initially intended or microtome stopped in mid-cut (LASIK only)”  
 To: “H. Misaligned flap (LASIK only)”
- I. In Sections 3.2.1. and 3.2.2., change “These endpoints and target values are based primarily on recommendations of the Ophthalmic Devices Panel. However, these endpoints and values are only guidance.” To: “Endpoints and target values should be evaluated following the primary treatment plus all planned enhancements.

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### ASTIGMATISM ISSUES FOR DISCUSSION

- A. Is vector analysis needed for all eyes treated for astigmatism, or only for eyes with BSCVA loss or complications?
- B. For eyes treated for astigmatism, what effectiveness criteria are needed in addition to those recommended for other indications? Should effectiveness criteria include both vector analysis and absolute magnitude with axis shift? How should these data best be presented? Is the following example an optimal categorization of clinically relevant data?

Residual Cylinder	Shift in Axis
0 - 0.5	> <u>±</u> 30
0.51 - 1.0	<u>±</u> 30
1.01 - 2.0	<u>±</u> 15
2.01 - 3.0	<u>±</u> 10
>3.01	<u>±</u> 5

## REVISED TABLES FOR ALL INDICATIONS

### Definitions of Major Safety Endpoints and Target Values:

Safety Target Values (Criteria are the same for surface or intrastromal ablation)	Low to Moderate Myopia (less than or equal to 7D SE) with/without astigmatism	High Myopia (greater than 7D SE) with/without astigmatism	Hyperopia with/without astigmatism
Percent of eyes losing more than 2 lines of best spectacle corrected visual acuity (BSCVA )	<5%	<5%	<5%
Percent of eyes that have BSCVA worse than 20/40 (BSCVA 20/20 or better preoperatively)	<1%	<1%	<1%
Percent of eyes with induced manifest refractive astigmatism of greater than 2.0 D of absolute cylinder power	<5%	<5%	<5%
Percent of eyes with adverse events (per type of event) <sup>1</sup>	<1%	<1%	<1%

1. The frequency of miscreated flaps may exceed 1%.

Note 1. Endothelial cell loss is an additional safety endpoint that needs to be evaluated when laser refractive surgery is performed closer than 200 microns from the corneal endothelium or the laser parameters (e.g., wavelength and fluence) used are likely to damage the endothelium.

Note 2. Contrast sensitivity loss with and without glare are additional safety endpoints that may need to be evaluated when ablation parameters are likely to compromise visual performance (See Appendix B). Additionally, all laser refractive surgery subjects should be provided with appropriate precautionary language regarding potential contrast sensitivity loss in the informed consent during the IDE study and the device should be labeled with such precautionary language after PMA approval.

**Definitions of Effectiveness Endpoints and Target Values:**

Effectiveness End Points and Target Values (Criteria are the same for surface or intrastromal ablation)	Low to Moderate Myopia (less than or equal to 7D SE) with/without astigmatism	High Myopia (greater than 7D SE) with/without astigmatism	Hyperopia with/without astigmatism
Percentage of eyes with UCVA 20/40 or better (BSCVA 20/20 or better preoperatively)	85%	75%	85%
Percentage of eyes that achieve predictability (attempted versus achieved) of the manifest refraction spherical equivalent of $\pm 2.00D$	NA	90%	NA
Percentage of eyes that achieve predictability (attempted versus achieved) of the manifest refraction spherical equivalent of $\pm 1.00D$	75%	60%	75%
Percentage of eyes that achieve predictability (attempted versus achieved) of the manifest refraction spherical equivalent of $\pm 0.50D$	50%	30%	50%
Percentage of eyes that achieve stability of the manifest refraction.	95%	95%	95%

**Inclusion Criteria:**

Inclusion Criteria (Criteria are the same for surface or intrastromal ablation)	Low to Moderate Myopia (less than or equal to 7D SE) with/without astigmatism	High Myopia (greater than 7D SE) with/without astigmatism	Hyperopia with/without astigmatism
Subjects should be 18 years of age or older	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
State refractive criteria (include spherical and cylindrical components)	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Minimum BSCVA in both eyes	20/40	20/60	20/40
Contact Lens Wearers <sup>1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Amount by which manifest refraction should progress during the year prior to the baseline exam.	≤0.50 D of Sphere or Cylinder	≤20% of Spherical Equivalent	NA
Subjects should be willing and capable of returning for follow-up examinations for the duration of the study.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Videokeratography should be normal.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Eyes with difference between cycloplegic and manifest refraction less than 0.75 D <sup>2</sup>	NA	NA	<input checked="" type="checkbox"/>

1. Contact lens wearers should remove soft or gas permeable contact lenses at least three days prior to baseline measurements. At that exam cycloplegic and manifest refractions as well as corneal topography should be obtained on both eyes. If the investigator determines that the topography is within normal limits, surgery may be scheduled at least one week after the initial exam, with no contact lens wear permitted prior to the surgery. If, on the day of scheduled surgery for the primary eye, central keratometry readings and manifest refraction spherical equivalents do not differ significantly from the initial exam measurements (by more than 0.50 diopter for low to moderate myopia and hyperopia, or by more than 1.0 diopter for high myopia), surgery can proceed. If the refractive change exceeds this criterion, the surgery should be rescheduled after refractive stability is achieved.

For fellow eyes, contact lens wear is permitted until at least three days prior to surgery. If, on the day of scheduled surgery for the fellow eye, central keratometry readings and manifest refraction spherical equivalents do not differ significantly from the initial exam measurements (by more than 0.50 diopter for low to moderate myopia and hyperopia, or by more than 1.0 diopter for high myopia), surgery can proceed. If the refractive change exceeds this criterion, the surgery should be rescheduled after refractive stability is achieved.

2. If subjects with latent hyperopia of 0.75 D or greater are to be studied, they should

be given the opportunity to participate in a contact lens trial to determine their tolerance to correction of full cycloplegic error while not under cycloplegia. The informed consent document should specify that future retreatment may be necessary if only the manifest refractive error is corrected.

### Exclusion Criteria

Exclusion Criteria (Criteria are the same for surface or intrastromal ablation)	Low to Moderate Myopia (less than or equal to 7D SE) with/without astigmatism	High Myopia (greater than 7D SE) with/without astigmatism	Hyperopia with/without astigmatism
Any residual, recurrent, or active ocular disease or corneal abnormality	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Signs of keratoconus	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Taking systemic medications likely to affect wound healing, such as corticosteroids or antimetabolites	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Previous intraocular or corneal surgery of any kind in the eye to be treated	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Immunocompromised or carrying diagnosis of connective tissue disease, clinically significant atopic disease or diabetes	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Unstable central keratometry readings with irregular mires	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Known sensitivity to study medications.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
History of glaucoma or glaucoma suspect .	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Participation in other ophthalmic clinical trials during this clinical investigation.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
History of herpes simplex or herpes zoster keratitis	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Women who are pregnant or nursing or who plan to become pregnant over the course of this clinical investigation.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Subjects at risk for angle closure	NA	NA	<input checked="" type="checkbox"/>
Subjects at risk for developing strabismus posttreatment	NA	NA	<input checked="" type="checkbox"/>

## EXAMINATION SCHEDULE

	PRE-OP	OP	D1 <sup>1</sup>	W1	M1	M3	M6	Final Exam <sup>2</sup>
Subject information, current medications, complications and adverse events	LM HM HP	LM HM HP	LM HM HP	LM HM HP	LM HM HP	LM HM HP	LM HM HP	LM HM HP
Distance UCVA	LM HM HP		LM HM HP	LM HM HP	LM HM HP	LM HM HP	LM HM HP	LM HM HP
Distance BSCVA <sup>3</sup>	LM HM HP			LM HM HP				
Manifest Refraction <sup>4</sup>	LM HM HP	LM HM HP <sup>5</sup>		LM HM HP				
Cycloplegic Refraction	LM HM HP							LM HM HP
Near UCVA	LM HM HP					HP		LM HM HP
IOP	LM HM HP			LM HM HP				
Slit Lamp Exam <sup>6</sup>	LM HM HP		LM HM HP	LM HM HP	LM HM HP	LM HM HP	LM HM HP	LM HM HP
Pupil Size <sup>7</sup>	LM HM HP				LM HM HP	LM HM HP	LM HM HP	LM HM HP
Dilated Fundus Exam	LM HM HP							LM HM HP
Pachymetry, keratometry <sup>8</sup>	LM HM HP	LM HM HP <sup>5</sup>						
Topography <sup>9</sup>	LM HM HP					LM HM HP	LM HM HP	
Patient Questionnaire <sup>10</sup>	LM HM HP					LM HM HP	LM HM HP	LM HM HP

LM = Low to Moderate Myopia (less than or equal to 7D SE) with/without astigmatism

HM = High Myopia (greater than 7D SE) with/without astigmatism

HP = Hyperopia with/without astigmatism

### Notes for the Examination Schedule

1. The same parameters are to be measured at each examination performed until re-epithelialization occurs.
2. The final exam should be conducted at least three months after the time when refractive stability is achieved. IDE studies for new indications (e.g., hyperopia and high myopia) should initially be proposed for 24 months follow-up, with the option to shorten follow-up time if satisfactory stability can be demonstrated earlier.
3. If the visual acuity with spectacle correction is  $\geq 2$  lines below that obtained preoperatively, a hard contact lens over refraction should be performed to determine the effect of irregular astigmatism and to estimate the best possible corrected visual acuity.

4. Manifest refractions for hyperopia should be conducted using a standard procedure that “pushes plus”, i.e., maximizes the hyperopic correction acceptable to the subject.
5. To be performed for contact lens wearers (see note 1 under inclusion criteria).
6. The slit lamp exam should include a complete survey of the anterior segment. The cornea should be examined in detail with specific recordings and gradings ( 0 to 4+ scale, 0=clear) of the following information: overall corneal clarity, any abnormalities such as corneal infiltrates, opacities in the lamellar bed and density of the scar around the edge of the flap (for LASIK).
7. Pupil size should be assessed under dim conditions at the preop exam and one of the following: following discontinuation of steroids, at time of stability or final exam.
8. Pachymetry, keratometry and axial length should be assessed on all eyes preoperatively and if needed to assess anomalous results in the postoperative course
9. Topography should be performed at the pre-op exam and at the time of anticipated stability.
10. The questionnaire should be administered at the preop exam, at the time of anticipated stability and at the final exam. It should include questions regarding mesopic conditions (including but not limited to night driving). The analysis of study results should attempt to correlate haze to problems identified by subjects under mesopic conditions.

## Appendix A.

### EXAMINATION SCHEDULE

	PRE (Both eyes to be examined.)	OP	D1	RE- EP	W1	M1	M3	M6	M9	M12	M18	M24
Patient's name, exam date and time, investigator's name, subject's ID #, operative eye, current medications	X	X	X	X	X	X	X	X		X	X	X
Patient's birth date, sex, race, PMHx, POHx, contact lens hx, refraction stability	X											
Distance UCVA	X		X	X	X	X	X	X	X	X	X	X
Distance BSCVA <sup>1</sup>	X				X	X	X	X	X	X	X	X
Manifest Refraction	X				X	X	X	X	X	X	X	X
Cycloplegic Refraction	X							X		X		X
Near UCVA	X				X	X	X	X		X	X	X
Near BSCVA	X							X		X		X
IOP	X				X	X	X	X	X	X	X	X
Slit Lamp Exam <sup>2</sup>	X		X	X	X	X	X	X	X	X	X	X
Pupil Size <sup>3</sup>	X		X	X	X	X	X	X	X	X	X	X
Dilated Fundus Exam	X							X		X		X
Pachymetry, keratometry, axial length <sup>4</sup>	X											
Topography	X					X	X	X		X		X
Patient Questionnaire <sup>5</sup>	X				X	X	X	X	X	X	X	X
Adverse Events / Complications		X	X	X	X	X	X	X	X	X	X	X

## Notes for the Examination Schedule

1. If the visual acuity with spectacle correction is  $\geq 2$  lines below that obtained preoperatively, a hard contact lens over refraction should be performed to determine the effect of irregular astigmatism and to estimate the best possible corrected visual acuity.
2. The slit lamp exam should include a complete survey of the anterior segment. The cornea should be examined in detail with specific recordings and gratings (0 to 4+ scale, 0=clear) of the following information: overall corneal clarity, any abnormalities such as corneal infiltrates, opacities in the lamellar bed and density of the scar around the edge of the flap (for LASIK).
3. Pupil size should be assessed whenever VA measurement is done
4. Pachymetry, keratometry and axial length should be assessed on all eyes preoperatively and if needed to assess anomalous results in the postoperative course
5. The questionnaire should include questions regarding mesopic conditions (including but not limited to night driving). The analysis of study results should attempt to correlate haze to problems identified by subjects under mesopic conditions.”