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The American Academy of Ophthalmology Task Force for Developing Novel End Points for Premium Intraocular Lenses members include: Jack T. Holladay, MD, MSEE, Chair; Adrian Glasser, PhD, Co-Chair; Scott MacRae, MD, Co-Chair; Samuel Masket, MD; Walter Stark, MD; and the following U.S. Food and Drug Administration staff members: Malvina Eydelman, MD; Don Calogero, MS; Gene Hilmantel, OD; Eva Rorer, MD; Tieuvi Nguyen, PhD; and Michelle E. Tarver, MD, PhD.

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Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses

In 1978, the US Food and Drug Administration approved the first investigational device exemption studies of intraocular lenses (IOLs). Outcomes were initially published in 1983 on pooled, publicly available data from IOL premarket approval studies that were used to support marketing approvals.[1] After publication, this "historical control" information was used as a benchmark for the assessment of the safety and effectiveness of new IOLs. These safety and effectiveness endpoints have been referred to as the "Food and Drug Administration Grid" and "Safety and Performance Endpoints" (SPEs) for IOLs. Although the SPEs were updated on the basis of additional premarket approvals in 1998, they have not been updated to reflect the development of "premium IOLs," including toric, multifocal, accommodative, and phakic IOLs.[2] Premium IOLs may present additional adverse events (AEs) to those already established for monofocal IOLs. Further, most of the AEs in the "Grid" do not have standard definitions, and the definitions used could have changed over time with advances in our understanding of ocular pathology. Considering untoward events associated with premium IOL implantation and that would be appropriate as safety endpoints in clinical studies of new premium IOLs, the American Academy of Ophthalmology's Task Force has developed consensus definitions for premium IOL SPE AEs as shown in Table 1. The AE of secondary IOL intervention has been subcategorized by the type of intervention and IOL exchange, removal, and reposition. These indications are listed and defined in Table 2 and Appendix 1.

At this time, acceptable rates for premium IOL SPE AEs have not been established. However, the definitions proposed may be used during clinical studies of new IOLs going forward to allow for the determination of appropriate SPE rates that can be applied to the assessment of new premium IOLs in the future.

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Table 1. Postoperative Adverse Event Definitions for Intraocular Lenses

Adverse Event	Definition
Chronic anterior uveitis	Persistent anterior segment inflammation characterized by grade 1+ cell or greater using SUN criteria[3]
Clinically significant cystoid macular edema	Macular edema diagnosed by clinical examination and adjunct testing (e.g., OCT, FA) resulting in BCDVA of ≤20/40 at ≥1 mo
Corneal edema	Corneal swelling (stromal or epithelial) resulting in BCDVA of ≤20/40 at ≥1 mo
Endophthalmitis	Intraocular inflammation requiring diagnostic vitreous tap and intraocular antibiotics
Mechanical pupillary block	Shallowing of anterior chamber due to obstruction of aqueous humor flow from the posterior to anterior chamber through the pupil by the crystalline lens, vitreous face, or implanted device
Increased IOP	Elevation of IOP by ≥10 mmHg above baseline to a minimum of 25 mmHg
Rhegmatogenous RD	Partial or complete RD associated with retinal tear
Toxic anterior segment syndrome	Acute, noninfectious inflammation of the anterior segment that starts within 24 hrs after surgery, usually resulting in hypopyon and commonly presenting with corneal edema, that improves with steroid treatment
Secondary IOL intervention	
Exchange	The investigational device is replaced with the same lens model.
Removal	The investigational device is removed and replaced with a noninvestigational lens or no lens is implanted.
Reposition	The existing IOL is surgically moved to another location or rotated.

BCDVA = best-corrected distance visual acuity; FA = fluorescein angiography; IOL = intraocular lens; IOP = intraocular pressure; OCT = optical coherence tomography; RD = retinal detachment; SUN = Standardization of Uveitis Nomenclature.

Table 2. Definitions of Indications for Device Exchange, Removal, or Reposition

Indication	Definition
Capsular block syndrome	Hyper-distention of the lens capsular bag due to the IOL optic blocking egress of fluid through the anterior capsulotomy typically inducing a myopic refractive error
Cataract	Any opacification of the crystalline lens with or without reduced visual acuity
Chronic anterior uveitis	Persistent anterior segment inflammation characterized by grade ≥1+ cell using SUN criteria[3]
Endothelial cell loss	Chronic endothelial cell loss at a rate greater than that due to normal aging
Incorrect IOL power	Postoperative refractive error different from predicted and not due to a calculation or other user error
Iris pigment epithelium loss*	New or worsening iris transillumination defects or increase in pigmented cells in the anterior chamber noted after the 1-wk visit when assessed before instillation of any dilating drops
Lens optic abnormality	Unanticipated visual outcome (e.g., acuity, contrast sensitivity, symptoms) associated with opacification, vacuoles, microvacuoles, or subsurface nanoglistenings and not due to other causes
Malpositioned IOL	Decentration, tilt, or rotation of IOL requiring reoperation May include changes induced by Nd:YAG laser anterior or posterior capsulotomy
Early	If noted before 120 days postoperatively
Late	If noted at ≥120 days postoperatively
Damaged IOL	Crack of lens optic, breakage, or deformity of haptic, or other damage to the IOL May include changes induced by Nd:YAG laser anterior or posterior capsulotomy
Pupil ovalization	Progressive deformation of the pupil with elongation of the pupil in the meridian of the long axis of the IOL Documentation to be made under photopic conditions†
Pain	Graded as ≥4 on the standardized pain numeric rating scale of current pain intensity from 0 (no pain) to 10 (worst possible pain)
Peripheral anterior synechiae	Progressive closure of the anterior chamber angle due to propagation of anterior synechiae in the absence of obvious anterior uveitis
Patient-reported undesirable optical phenomena	Dysphotopsia (positive or negative or both), monocular diplopia, intolerable glare, halos, or other visual symptoms, not due to 1 of the indications listed

IOL = intraocular lens; Nd:YAG = neodymium-doped yttrium aluminium garnet; SUN = Standardization of Uveitis Nomenclature.
*If there is a transillumination defect preoperatively, then a photograph should be taken, and then at each subsequent visit, a photograph should be taken and compared with the preoperative photograph via a standardized photographic method.
†A consensus statement regarding a proposed methodology for standardizing assessment of pupil ovalization is available in Appendix 1.

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Appendix 1. Oval Pupil Measurement Background and Standard Operating Procedure

Background

The only study of the oval pupil available was by Isotani et al[3] in 1995, who studied the ratio of the major to minor diameter in healthy subjects by using infrared photography. The subjects were dark adapted, so these are scotopic pupil measurements.

Standard Operating Procedure

If the clinician observes an oval or irregularly shaped pupil (dyscoria) at any visit after surgery, photographs should be taken at that visit and each subsequent visit to determine if the ovalization is progressive. The major and minor diameters of the pupil, which may not be orthogonal, are measured on the photograph, which must be taken in photopic conditions (>200 foot-candles or 2153 lux) so the pupil is maximally constricted. The pupil constriction provides the setting for pupil ovalization. For the measurement, the diameters must pass through the center of the least-squares, best-fit ellipse or centroid of the pupil perimeter. The ratio of the major to minor diameter is then calculated and reported. The photograph may be taken with any camera, including but not limited to slit-lamp cameras, topographers, and Scheimpflug devices, but the eye image must be captured under photopic conditions as specified.

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Special Report: American Academy of Ophthalmology Task Force Summary Statement for Measurement of Tilt, Decentration, and Chord Length

Currently, the measurement of tilt and decentration is not commercially available in an instrument or method that has been validated clinically. In lieu of a validated, commercially available instrument or method, the current statuses of 3 different approaches that have been used to measure tilt and decentration are described to help provide the basis for the future development of an instrument or technique.

Definitions

- Decentration of an intraocular lens (IOL) is the lateral horizontal and vertical displacement of an IOL relative to the visual axis as seen by the clinician through the cornea (subject-fixated coaxially sighted corneal light reflex, as described by Chang and Waring[1]).
- Tilt of an IOL is the horizontal and vertical angle from perpendicular of an IOL relative to the visual axis (subject-fixated coaxially sighted corneal light reflex, as described by Chang and Waring[1]).
- Chord length μ is the displacement (distance) between the subject-fixated coaxially sighted corneal light reflex and pupil center.[1] For some diffractive IOLs, the midpoint between pupil center and visual axis may be optimal.

Tilt, Decentration, and Chord Length μ

The goal is to measure tilt, apparent decentration through the cornea, and chord length μ on all subjects with a premium IOL.

Table 1. Ratio of IOL Toricity to Corneal Astigmatism

	Effective Lens Position					
A-constant—>	116.346	117.203	118.059	118.916	119.773	120.630
Surgeon Factor—>	0.287	0.772	1.257	1.742	2.227	2.713
ELP—>	4.000	4.500	5.000	5.500	6.000	6.500
IOL Power	Resulting Ratio of IOL Toricity to 2 D of Corneal Astigmatism					
10	1.359	1.424	1.494	1.571	1.654	1.745
22	1.277	1.330	1.387	1.450	1.519	1.595
34	1.198	1.239	1.284	1.334	1.390	1.452
46	1.121	1.151	1.185	1.223	1.267	1.316

D = diopter; ELP = effective lens position; IOL = intraocular lens.