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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: American Academy of Ophthalmology Task Force Recommendations for Specular Microscopy for Phakic Intraocular Lenses

The American Academy of Ophthalmology Task Force Consensus Statement on Specular Microscopy for investigational phakic intraocular lenses provides more detail than currently available guidelines on the management of specular microscopy evaluations to ensure subject safety during the clinical investigation of new phakic intraocular lenses (PIOLs). Although these recommendations were written for PIOLs, similar safety principles could be used for pseudophakic intraocular lenses in studies that require subject follow-up for similar or shorter durations. Specular microscopy is an important prognostic test that allows clinicians to identify unacceptable progressive corneal endothelial cell loss rates and potentially remove an offending implant before the damage causes irreversible corneal edema.[1] These studies are critical not only to demonstrate the overall safety of the device being evaluated for the general population but also to protect participating study subjects.[2,3]

Although current American National Standards Institute (ANSI) guidelines exist for PIOL studies, these do not describe how the investigators should be notified and how they should follow subjects showing significant losses during the trial. Therefore, we have specified some recommendations concerning how information should pass between sponsors of such new PIOLs, reading centers, and the investigations, so that subject safety is adequately protected.

Consensus Statement

Endothelial Cell Data

Specular microscopy should be performed preoperatively and at the 6-, 12-, 24-, and 36-month postoperative intervals (at a minimum). A minimum of 6 scans with good images should be performed at the preoperative visit and a minimum of 3 scans with good images should be performed at each postoperative visit. Care should be taken to minimize artifacts caused by dry eye or a poorly focused image. The proportion of eyes with $\geq$25% endothelial cell loss from preoperative cell density should be considered an end point for a clinical investigation of a new PIOL.

A $\geq$20% endothelial cell loss or an endothelial cell count of $<$1500 cells/mm^2 should trigger recalling the subject and retesting the specular microscopy to confirm the cell loss or count.[1] Serial specular microscopies can be performed on eyes of concern every 4 to 6 months to evaluate the cell density stability. For these eyes, if there appears to be an accelerated annual cell loss rate above 1%/year, then implant removal may be considered.

The reading center should read the specular microscopy images and report the cell count in cells/mm^2 to the sponsor of a clinical investigation within 90 days of when specular microscopy is performed, so that the sponsor can analyze the percentage increase or decrease in cell density compared with preoperative readings. The sponsor should notify the investigator within 30 days of receiving a reading center report if the endothelial cell density decreases 20% or more from the preoperative value or falls below 1500 cells/mm^2. The sponsor should also report annually to the investigator any eyes that have a 15% or higher cell density decrease from the preoperative value.

Specular microscopy imaging systems using validated manual counting methods are currently standard for such studies. The ANSI Z80.13 Phakic Intraocular Lenses standard (clause D.4.2) provides detailed recommendations to minimize the variability of specular microscopy measurements.

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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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