



Limitations of Existing Endpoints for Premium IOLs

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Disclosure

- No Financial Relationships to Disclose

IDE Study Approval vs. Available Study Recommendations

- **Monofocal IOLS:**
 - » FDA recognized ANSI/ISO standards
 - Preclinical and clinical recommendations clearly delineated
 - » 71% total IDEs (FY'05-FY'12) were approved or approved with conditions within first round

- **Premium IOLs:**
 - » Few recognized ANSI/ ISO Standards
 - Several endpoints not clearly delineated
 - » 39% total IDEs (FY'05-FY'12) were approved or approved with conditions within first round

Aphakic Monofocal IOL Investigations (ISO 11979-7)¹

- **Effectiveness**

- » Best Corrected Visual Acuity (BCVA)

- **Safety**

- » Safety and Performance Endpoints (SPE²) rates for Adverse Events (AEs)

- | | |
|-----------------------------------|-------------------------|
| ▪ corneal edema | ▪ cystoid macular edema |
| ▪ hypopyon | ▪ pupillary block |
| ▪ intraocular infection | ▪ retinal detachment |
| ▪ secondary surgical intervention | ▪ iritis |
| ▪ raised IOP requiring treatment | |

- » IOL tilt / Decentration

¹ FDA Recognized Standard

² Basic historical safety and effectiveness data (FDA Grid) incorporated in ISO 11979-7

Phakic Monofocal IOL investigations (ISO 11979-10, ANSI Z80.13)¹

Effectiveness – BCVA plus:

- Best Distance Corrected Near Visual Acuity
- Uncorrected Near Visual Acuity (ANSI only)
- Uncorrected Distance Acuity (UCDA)

Safety – SPE plus:

- Endothelial Cell Loss
- IOL Tilt / Decentration
- Contrast Sensitivity
- Crystalline lens status
- Clearance analysis (e.g., IOL-cornea)
- Subject Questionnaire
- AEs related to IOL design

¹ FDA Recognized Standards

Aphakic Multifocal IOL Investigations (ISO 11979-9 and ANSI Z80.12)¹

Effectiveness – BCVA² plus:

- Uncorrected Near VA, Uncorrected Distance VA²
- Distance Corrected Near VA (DCNVA)²
- Defocus curve (depth of focus)³

Safety – SPE plus:

- Explants for optical / visual reasons
- Mesopic DCNVA
- IOL Tilt / Decentration
- Contrast sensitivity⁴
- Fundus visualization
- Functional performance (night driving testing)⁴
- Subject Questionnaire (visual symptoms/aberrations)⁴

¹ FDA Recognized Standards

², Monocular and Binocular ; ³ Binocular ; ⁴Outcomes compared to a concurrently run monofocal IOL control group.

Toric IOL Investigations: Aphakic and Phakic (ISO 11979-7 DIS and ANSI Z80.30)

- **Effectiveness**¹ – BCVA plus:
 - » Evaluation of Cylinder
 - refractive cylinder, IOL misalignment, IOL rotational stability, pre-op and postop keratometry
 - » UCVA

- **Safety** – SPE plus:
 - » IOL Tilt / Decentration
 - » Subject Questionnaire (visual symptoms/aberrations)²

¹ Effectiveness Outcomes are compared to those associated with a concurrently run non-toric IOL (similar design) control group for the lowest power only

² For ISO only, if necessary based on risk analysis

Aphakic Accommodative Investigations (ISO 11979-7 DIS and ANSI Z80.30 (Draft))

Effectiveness – BCVA plus:

- Distance, Intermediate, Near UCVA
- Intermediate and Near VA with Best Correction for Distance
- BCNVA and Add Power
- Accommodative Amplitude (AA) (objective testing, 1 D min.) /
Assess AA Stability

Safety – SPE plus:

- IOL Tilt / Decentration
- Contrast Sensitivity
- Subject Questionnaire
- AEs related to IOL design

Limitations of Current Standards for Premium IOLs

- **Performance Criteria**

- » SPE

- Key safety outcome in all standards
- Entry of premium IOLs to the marketplace highlight limitations (e.g., different rates of secondary surgical interventions)

- **Testing**

- » Some recommended tests for “Premium” IOLs do not have well established methodologies

- IOL tilt/decentration
- Objective method for anterior subcapsular cataract and posterior capsular opacification
- Accommodation
- Functional performance (e.g. reading speed, night driving)
- Patient Reported Outcomes

Introduction of Extended Depth of Focus (EDOF) IOLs

- New Category of IOLs for Improved Near and Intermediate Performance
- No current standards or draft standards
- No guidance
- Today – the first public discussion of probable requirements for preclinical and clinical testing

Today's Focus on Areas with Highest Impact

- Premium IOL Safety Assessments
- Patient Reported Outcome (PRO) Measures
- Objective Assessments of Accommodation
- Subjective Assessments of Accommodation and EDOF

Premium IOL Safety Assessment

Concerns with historical adverse event (AE) rates currently used as safety benchmarks:

- May not reflect current standard cataract surgery instrumentation and techniques
- Different types of AEs with premium IOLs
- Acceptable rates of AEs with premium IOLs may be different
 - » Different risks/benefits for premium vs. monofocal IOLs

Patient-Reported Outcomes (PROs)

- Concerns with currently used questionnaires
 - » Have not undergone psychometric evaluation
 - » Have not been evaluated for validity in the intended population
 - » Have not robustly shown that the scores are meaningful
 - » Have not been developed and evaluated for some concepts of interest

Assessment of Accommodation

- Limitations of subjective assessments:
 - » Cannot distinguish true accommodation from pseudo-accommodation
 - » Affected by multiple non-specific factors → bias (overestimates)
- Objective assessments – outstanding issues:
 - » Optical: Can they be used with all lenses?
 - » Biometric: difficulties with ocular fixation, stimulation of accommodation, and conversion to optical diopters
 - » Need standardization of procedures?
- ANSI/ISO standards call for objective measurements to minimize limitations of subjective assessments

Subjective Assessment of Accommodation and Extended Depth of Focus (EDOF)

- Concerns with subjective evaluations of accommodation and depth of focus
 - » Current subjective methods
 - may not be adequate to differentiate true performance difference from placebo effect (e.g., effects of patient squinting, blur interpretation)
 - may not accurately assess accommodation
- In EDOF subjects - manifest refractions may have high variability
- No current standards or guidance exist to assist in the development of EDOF IOLs

Development of Endpoints for Premium IOLs



The Fastest Route To Market

