Aberration Analyses Needed for FDA Evaluation of Safety and Effectiveness of Wavefront-guided Refractive Surgical Devices

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Introduction

- FDA perspective on evaluating new medical devices.
- Surgical treatments of aberrations of the eye illustrate difficulties of evaluating cutting-edge technology before basic science is known.
- FDA must sometimes develop new tests, analyses and criteria to evaluate marketing applications.
- Healthy interactions among regulatory, industrial, medical and scientific communities are critical to efficient development of new medical technology.
FDA Perspective

- FDA is responsible for evaluating the safety and effectiveness of new devices, regardless of whether appropriate evaluation techniques are available.

- “Reasonable assurance of safety and effectiveness” must be based on valid scientific evidence.

- Evidence is needed to support claims for intended use as well as device performance.

- FDA bases judgments on all available information, but can require only the information and analyses needed to determine safety and effectiveness.

- FDA uses established tests and analyses where possible, but must sometimes develop new ones.
Evaluating Aberrations of the Eye

- Defocus and Astigmatism: “conventional” aberrations
- Corneal topography and Aberrometry: New methods for measuring coma, spherical aberration, other “higher order” aberrations
Evaluating Defocus and Astigmatism

- **Tests**
  - Manifest Refraction
  - Visual Acuity
  - Subjective Questionnaire
  - Mesopic Contrast Sensitivity

- **Analyses**
  - Refractive Stability
  - Vector Analysis for Astigmatism
  - Predictability
Evaluating Defocus and Astigmatism

- **Safety Measures and Criteria**
  - Maintenance of best-corrected visual acuity.
  - Low incidence of “adverse events”
  - Low incidence of “subjective symptoms”

- **Effectiveness Measures and Criteria**
  - Accuracy of manifest refractive correction.
  - Stability of manifest refractive correction.
  - Improvement of uncorrected visual acuity
Evaluating Higher Order Aberrations

- **Tests**
  - Conventional Tests
  - Wavefront Measurement
  - Corneal Topography

- **Analyses**
  - Conventional Analyses
  - Zernike Analysis (Large and Small Pupils)
  - Equivalent Defocus Analysis
  - RMS Deviation Analysis
  - Corneal/Internal Aberration Analysis
  - Point Spread Functions
Evaluating Higher Order Aberrations

- Safety Measures and Criteria
  - All Conventional Measures
  - Conventional measures no worse than after conventional refractive surgery
  - Aberrations no worse than after conventional surgery
  - Contrast sensitivity no worse than after conventional surgery
Evaluating Higher Order Aberrations

- Effectiveness Measures and Criteria
  - Conventional Measures
  - Compare Preop BSCVA to Postop UCVA
  - Compare Wavefront Defocus to MRSE
  - Aberration Reduction (Overall and Individual Zernike Terms)
  - Aberration Stability
  - Compare Large & Small Pupil Aberrations
Limitations of Higher Order Aberration Treatments

- Corrections are small, close to the precision limit of the laser.
- Visual benefits are relatively small and hard to measure.
- Small positioning errors can greatly affect outcome.
- Uncontrolled Corneal Changes
  - Biomechanical effects
  - Healing effects
  - Normal variability and aging changes
Unanswered Questions About Higher Order Aberrations

- **Spherical Aberration**
  - How much is optimal for vision?
  - What are the functional differences between positive and negative?
  - How does it contribute to depth of focus and accommodation?

- **Coma**
  - How much is optimal for vision?
  - What are the visual effects of axis orientation and axis shift?
How can we distinguish postoperative recovery changes from:

- Normal Variations
- Tear Film Changes
- Accommodative Changes
- Pupil Size Changes
- Lens Changes and Variations in Corneal/Lenticular Balance
Unanswered Questions about Higher Order Aberrations (cont)

- Cornea-Lens Aberration Interactions:
  - Is the corneal compensation of lens aberrations dynamic?
  - Is it better to correct the wavefront or the front corneal surface?
  - Does epithelial remodeling nullify corneal aberrations induced to compensate for lens aberrations?
Unanswered Questions about Higher Order Aberrations (cont)

- **Therapeutic Treatments**
  - How can we evaluate treatment of localized irregularities where Zernike analysis fails?
  - Should treatments be wavefront-based or topography-based?
  - Should calibration requirements be more stringent for treatment of local irregularities (very high order aberrations)?
For proper evaluation of device safety and effectiveness, key variables, measurement methods, analyses and criteria should be established through basic research and preclinical studies prior to clinical trials.

In the case of cutting-edge technologies, such as the surgical treatment of higher order aberrations of the eye, device manufacturers are motivated to conduct premarket clinical trials prematurely, before the fundamental facts are known and appropriate assessment tools are developed.
Summary (continued)

- I have outlined a number of areas in the evaluation of aberration treatments where important safety and effectiveness variables have been identified, but basic knowledge is incomplete and adequate assessment tools have not been developed.

- The FDA does not have the resources or the authority to carry out the necessary research and development, but the basic vision and ophthalmology research community does. The exciting research being presented at this meeting shows that the research community recognizes these needs, and is forging ahead to meet them.
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