W

hile hundreds of mono-
focal intraocular lenses
(IOLs) are on the U.S. market, only 10 of the
so-called “premium IOLs” are available. Why is it taking
so long to get more of these lenses ap-
proved? And are there ways to expedite
the process? The Academy and the U.S.
Food and Drug Administration (FDA)
explored these questions and more in a
first-ever collaborative workshop held
this spring.

More than 230 clinicians, re-
searchers, FDA leaders, and industry
representatives met to discuss novel
depth of focus
 endpoints for premium IOLs, covering
such topics as adverse events (AEs),
methods for assessing visual distur-

bances, and surgeons’ expectations for
IOLs providing near vision. In addi-
tion, they discussed a new type of IOL
known as the extended depth of focus
IOL (see “New Kid on the Block”).

Here’s an overview of the daylong
proceedings, including highlights from
the individual breakout sessions.

The Road to Approval

Today, approximately 14 percent of
cataract patients receive one of three
types of premium IOLs: accommodat-
ing, multifocal, or toric; a fourth type
of premium IOL is the phakic IOL.
(Although there is considerable con-
troversy in the ophthalmic community
about the term premium, this article
uses the nomenclature from the work-
shop.) The FDA has received an in-
creasing number of requests for review
of additional entries, but the process
for review is a cumbersome one.

“Currently we have a limited avail-
ability of FDA guidance or recognized
standards. As a result, we evaluate
many submissions on a case-by-case
basis,” said Malvina B. Eydelman, MD,
at the FDA. “Both the FDA and spon-
sors spend significant resources on re-
peat submissions, and there’s a delayed
or limited benefit to other devices with
similar characteristics.”
Existing roadblocks. Obstacles to approval include “a lack of consensus in some preclinical issues, on best clinical trial design, and [on] appropriate safety and effectiveness endpoints,” Dr. Eydelman said. Additionally, there is a need for new categories of IOLs, “based on new optical properties and/or benefits to patients,” she said.

Which way forward? “We can continue to evaluate each submission one at a time and take a long and winding road, or we can do what we’re trying to attempt [in this workshop]—develop the novel endpoints for premium IOLs,” Dr. Eydelman said.

Four Hot Topics
Clinicians and patients want a broader array of IOL options. Patients want to see as well as possible, and most want to minimize their dependence on spectacles. Physicians want safe products and happy patients. What measures might be used to guide IOL regulatory approvals and clinical decision making to best achieve those goals?

The workshop was organized around the following hot topics.

Safety issues. Premium IOLs have unique safety risks, “which are an inevitable trade-off for the added benefits that they provide,” said Douglas D. Koch, MD, at Baylor College of Medicine. “For example, with toric IOLs, there is the occasional occurrence of postoperative astigmatism due to problems with misalignment and postoperative IOL rotation; in rare instances, this requires surgical reinsertion to adjust the axis alignment.”

With multifocals, he noted, “Explants may be occasionally required due to complaints about loss of contrast sensitivity and development of visual disturbances.”

Because accommodating lenses must move and flex to function, Dr. Koch said that they “can present mechanical issues like Z syndrome and anterior or posterior dislocations. Patients can rarely experience glare and halos from a smaller optic zone and irregular astigmatism related to optic flexure.” As for phakic IOLs, he said, “There have been reports of increased risk of corneal decompensation, uveitis, and glaucoma.”

When FDA reviewers evaluate the safety and performance of a new IOL, they compare the number of patients with a particular AE to an allowed rate of cumulative and persistent AEs on what’s known as the FDA “grid” (its formal name is “Safety and Performance Endpoints”). But is the current FDA grid applicable to premium IOLs?

Breakout consensus. Participants felt that the current grid needs little alteration. They recommended better definitions of some AEs; suggested minor changes to address specific lenses (such as rotation for toric lenses and endothelial cell loss for phakic IOLs); and advised that patient-reported outcomes (PROs) such as halos, glare, and negative dysphotopsias be added.

Patient-reported outcomes. A PRO refers to any report on the status of a patient’s health that comes directly from the patient without interpretation by a clinician or anyone else. In outcomes studies, PROs are often used to measure the effect of an intervention on such factors as symptom impact, disability, treatment tolerability, treatment satisfaction, and health-related quality of life.

PROs are “really among the most important factors we should be considering,” said William H. Maisel, MD, MPH, at the FDA. “It is no coincidence that we’re focusing here on PROs because of the large subjective component to these devices.” If ophthalmologists focus only on functions such as visual acuity and contrast sensitivity, they may overlook patients’ thoughts, beliefs, and attitudes about their vision, several speakers pointed out.

During the workshop, participants discussed a number of issues to consider beyond the traditional statistical measures of precision, reproducibility, validity, and responsiveness. For instance, how best can the words patients use to describe visual phenomena (such as starbursts, comets, and halos) be parsed? Should a single PRO measure that encompasses all types of IOLs be developed? Finally, can a collaborative mechanism be built that would allow stakeholders to share the development costs of a PRO instrument?

Breakout consensus. Participants agreed that the concepts of subjective quality of vision and visual function are both important—and that they exist independently of a specific IOL technology. In addition, they agreed...
that a collaborative model for PRO development should be pursued.

**Objective assessment of accommodation.** Accommodating IOLs, which vary the focal power of the eye, have the potential to provide an extended range of vision without loss of contrast sensitivity. Although it is possible to measure accommodation objectively in a clinical study, doing so involves addressing a number of challenges, including the advantages and disadvantages of the instruments used.

Speakers discussed ANSI/ISO draft standards for objective assessments (such as dynamic aberrometry and dynamic autorefraction) of accommodating IOLs and questioned whether the field should be developing standard operating procedures for optical and biometric methods. (For instance, ANSI and ISO require 1 D of objectively measured accommodation for a device to be called an accommodative IOL.)

**Breakout consensus.** Participants arrived at a clear consensus that the range of premium IOL technologies was too great to justify development of standard operating procedures for objective assessments.

**Subjective assessment of accommodation.** A number of variables come into play during assessment of accommodation, from lighting conditions to the nuances inherent in the interaction between the examiner and the patient. Moreover, consensus is lacking on a number of issues, such as time for testing and whether testing should be binocular or monocular (or both).

Subjective and objective tests need to be correlated, speakers said—and the results need to be further correlated with any PRO questionnaires.

**Breakout consensus.** Participants presented myriad recommendations, including the need to establish a subjective methodology of testing with an emphasis on defocus curves. In addition, they recommended using adaptive optics to test eye models under varied conditions.

**Cautions and Conclusions**

Patients with such conditions as age-related macular degeneration, epiretinal membrane, keratopathy, optic neuropathy, or prisms in their spectacles might not benefit from certain premium lenses or might experience unwanted visual effects, speakers cautioned. And patient expectations must always be kept in mind: Many who had hoped to be rid of spectacles may find themselves needing some postoperative correction, speakers noted.

Overall, the workshop was “a game changer,” said Dr. Eydelman. And Thomas A. Oetting, MD, at the University of Iowa, agreed. “The FDA clearly wanted input from industry and surgeons. I felt that the meeting was indeed a ‘working’ workshop and that progress was made on developing assessments like PROs for premium IOLs.”

Next, the FDA and the Academy will work to determine a strategy for dealing with recommendations presented during the meeting, in conjunction with the National Eye Institute.

1 FDA/AAO Workshop on Developing Novel Endpoints for Premium IOLs, held March 28, 2014 in Silver Spring, Md.
2 For a full transcript of the session, see www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm365646.htm.

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