DRAFT CONSENSUS STATEMENT FOR COMMENT

October 7 2015

This statement was developed as a result of breakout group recommendations from the March 24, 2014 Developing Novel Endpoints for Premium IOLs Workshop held in Silver Spring, Maryland. The primary goal of the workshop was to improve the regulatory science for evaluating premium IOLs, which in turn may enhance the efficiency with which safe and effective premium IOLs get to the market.

We are indebted to the Task Force on Developing Novel Endpoints for Premium IOLs formed after the Workshop for developing these statements based on the workshop discussions and recommendations, available peer-reviewed scientific literature, and other expert opinions. The Task Force includes the following : Jack Holladay, MD, Chair; Adrian Glasser, PhD, Scott MacRae, MD, Samuel Masket, MD, and Walter Stark, MD. The FDA liaisons to this Task Force include the following: Malvina Eydelman, MD, Don Calogero, MS, Gene Hilmantel, OD, MS, Tieuvi Nguyen, PhD, RAC, Eva Rorer, MD, and Michelle Tarver, MD, PhD.

We would like to solicit broad input from industry and other interested parties.

Please send your comments, your affiliation and contact information with the title of the referenced document to hoskinscenter@aao.org by the following deadline: **November 10, 2015** Please note that comments received after close of the comment period will not be accepted.

**DRAFT AMERICAN ACADEMY OF OPHTHALMOLOGY TASK FORCE CONSENSUS STATEMENT ON
TESTING FOR EXTENDED DEPTH OF FOCUS INTRAOCULAR LENSES**

I. Testing for EDOF
   A. Criteria for EDOF IOLs (Minimum 100 eyes in study and control group)
      1. The defocus curve for the EDOF of IOL needs to have a depth of defocus of at least 0**.5 D** greater negative lens power than the defocus curve for the monofocal IOL control at log MAR 0.2 (20/32) [See Defocus Curve Testing Methodology, below.]
      2. Mean (logMAR) monocular distance-corrected intermediate visual acuity (DCIVA) under photopic conditions at 67 cm at 6 months. Demonstrate statistical superiority over the control [one-sided test using level of significance of 0.025]
      3. EDOF IOL needs to have at least 50% of eyes achieving DCIVA of better than or equal to logMAR 0.2 (20/32) at 67 cm.

   B. Additional considerations
      1. Best-Corrected Distance Visual Acuity. Compare the EDOF lens to the monofocal control with regard to monocular BCDVA, through a statistical non-inferiority analysis, using a non-inferiority margin of 0.1 logMAR.

      2. Defocus Curve Testing Methodology**.** A monocular defocus curve should be obtained by using the best corrected distance refraction and measuring the visual acuity in 0.5 diopter defocus steps between +1.50 D and -2.50 D, except for the region from +0.50 D through -0.50 D, which should be done in 0.25 D steps. Letters should be randomly presented to avoid memorization. The defocus range of +1.50 D to -2.50 D may be modified as applicable based upon lens design and expected depth of focus. The protocol should specify range of lens powers.
         a. The mean acuity across all eyes (in a study arm) should be calculated and plotted. The "depth of focus" is defined as the range of lens powers (from zero defocus to the largest negative power) over which the mean acuity is ≥ 0.2 logMAR.
         b. ANSI/ISO compliant visual acuity charts should have luminance of 85 cd/m2 +/- 10% with letters changed randomly between each change in trial lens power. Digitalized charts may be used according to the attached digital chart recommendations.
         c. The population mean, standard deviation, confidence intervals, and sample size calculation should be reported.
         d. The defocus data should also be grouped into three photopic pupil size ranges: ≤ 2.5 mm (small), >2.5 mm to <4.0 mm (medium), and ≥ 4.0 mm (large). Stratified analyses of "depth of

focus" and defocus curve plots should evaluate the effect of pupil size (f-stop, which uses apparent effective pupil size and effective axial length) on results.

e. All standard acuity, low contrast letter acuity and contrast sensitivity testing should conform to the surrounding luminance (in ISO 8596) which says acuity testing field has to extend to at least 0.5 degrees (area of background luminance), in the remaining surrounding field of <= 10 degrees the luminance must be > 10% but less than 25% and for > 10 degrees it must be >= 1%, but no greater than the value within the 10 degree field. Basically, the ROOM LIGHTS SHOULD BE OFF since this is variable, and a night light, tablet or iPad or other low light level conforming to above may be used.

3. <u>Mesopic Contrast Sensitivity testing must be performed with and without Glare Testing</u>. The gratings should avoid in rotational bias (vertical or horizontal). Low mesopic contrast sensitivity testing should be performed comparing test eyes to controls at 3 cd/m2 +/- 10% under mesopic conditions. The repeatability (precision) and sensitivity of the system should be at least +/- 2 dB (0.2 log units) for the contrast sensitivity function at 5 nominal spacial frequencies including (1.5, 3.0, 6.0, 12.0 and 18.0 cyc/deg). Digitalized charts may aid with sensitivity. The illumination at the eye of the glare source for mesopic testing should be 5.7 lux. A minimum of 4 glare sources at the plane of the target which are symmetrically spaced is recommended. The glare source(s) should be in the same plane as and between 3 to 15 ° from the center of the letter source (object). A small validation study should be performed to confirm that the glare parameters used are the minimum necessary to significantly reduce (e.g., 0.1 log units at one or more spatial frequencies) the contrast sensitivity of young adult subjects with normal vision.

4. <u>Intermediate Vision: Low contrast acuity at 67 cm (Distance-corrected)</u>. In order to help assess the quality of intermediate vision under sub-optimal conditions, the monocular 10% contrast letter acuity (DCIVA) at photopic light levels should be measured on each subject. Descriptive statistics (mean, standard deviation, median, maximum and minimum) should be provided for each arm. A low contrast letter acuity test under photopic conditions at a luminance of (nominally 85 cd/m2 +/- 10%) comparing test eyes to controls should be performed. The repeatability

(precision) and sensitivity of the system should be at leas +/- 2 dB (0.2 log units).