

**FDA Presentation and Questions:
Ophthalmic Devices Panel Meeting
August 1, 2002**

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Re: PMA P970043/S10, Alcon Laboratories Inc.,
CustomCornea™ LASIK with LADARVision™ 4000 Excimer Laser System
for correction of myopia up to -7.00D and astigmatism less than -0.50D at the spectacle plane.

FDA Review Team:

Jan Callaway (*team leader*)
Malvina Eydelman (*primary clinical*)
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Introduction:

Alcon has presented its request to market the LADARVision™ 4000 Excimer Laser System for wavefront-guided LASIK treatment of myopia, and has provided technical and clinical information to support its request. As detailed in Dr. Eydelman's clinical review, FDA has no significant clinical questions for the Panel regarding the safety and effectiveness of the device. The application is nevertheless important, because it is the first application for which the ablation pattern is determined entirely by objective wavefront measurements, and the treatment includes the attempted correction of higher order aberrations in addition to defocus and astigmatism. FDA therefore wishes to ask the Panel's advice about several issues specific to higher-order aberration treatments: the analysis and interpretation of the results, the information needed to support specific effectiveness claims, and the labeling information needed to communicate the expected results to patients and physicians.

Comparison of Clinical Outcomes of Custom and Conventional Treatments:

The outcomes of the 139-eye effectiveness cohort were compared to the outcomes of 47 conventionally treated eyes at 6 months after surgery. Comparison of wavefront-based (Custom) and conventional treatment clinical outcomes for low-contrast visual acuity, contrast sensitivity and higher-order aberrations shows that:

?? Mean higher-order aberrations were smaller after the Custom treatment than after the conventional treatment. Aberrations were smaller at 6 months than preoperatively for 38% of Custom eyes vs. 14% of conventional eyes. As estimated by comparisons of simulated

point spread functions and acuity chart images, the difference between Custom and conventional treatment image quality is roughly equivalent to a 0.2 diopter reduction of spherical refractive error.

- ?? Mean contrast sensitivity for Custom eyes improved by 0.1-0.2 log unit relative to conventional eyes.
- ?? Best-spectacle-corrected contrast sensitivity and low contrast acuity were both slightly better for the Custom eyes than for the conventionally treated eyes. The mean changes were small, but more Custom eyes showed clinically significant increases than decreases, whereas more conventional eyes showed clinically significant decreases than increases.

Question 1. What differences (if any) between Custom and conventional outcomes are clinically and/or functionally significant? What labeling claims are supported by these differences.

Question 2. Are additional clinical data, analyses or criteria needed to evaluate the relative effectiveness of Custom and conventional LASIK treatments with regard to higher order aberrations and visual function?

Analysis and Evaluation of Higher-Order Aberrations:

The functional significance of higher order aberrations and their relation to refractive error is often not evident. Tables of RMS error values for Zernike analysis coefficients may not adequately convey the effects of these errors on visual image quality. Some specific issues for consideration are:

- ?? Different Zernike terms with the same RMS error may have different effects on vision.
- ?? The Zernike coordinate system extends to the edge of the pupil; therefore, corneal maps of Zernike-defined aberrations change with changes in pupil size.
- ?? Elimination of all aberrations may not be optimal; e.g., some positive spherical aberration may be functionally beneficial.
- ?? New analysis methods may help to relate the functional effects of higher-order aberrations to more familiar measures of optical quality, such as defocus.

Question 3. What information about the measurement, analysis and correction of higher order aberrations is needed to accurately inform physicians and prospective patients about the safety and effectiveness of CustomCornea treatments?

Refractive Stability Criteria for Higher-Order Aberrations:

For conventional refractive surgery indications, current FDA criteria for refractive stability include:

- ?? Changes in refractive error should be ≤ 1.0 diopter for $\geq 95\%$ of eyes between 1 and 3 months or over a minimum 3-month period thereafter.
- ?? The mean rate of refractive change should be ≤ 0.5 diopter/year.
- ?? The rate of refractive change should be zero or decreasing toward zero at the time point of stability.
- ?? The 95% confidence interval around the mean change should include zero.
- ?? The time period immediately following stability should confirm criteria a-d above.

The existing stability criteria are insensitive to changes in higher order aberrations.

Question 4. What additional stability criteria should be defined for refractive surgical treatments of higher order aberrations?

The refractive effects of correcting higher order aberrations are smaller than the effects of correcting sphere and cylinder, suggesting that relatively modest instabilities of sphere and cylinder corrections could significantly disrupt higher order corrections.

Question 5. Should the criteria for stability of sphere and cylinder corrections be made more stringent for Custom treatments than for conventional treatments?