

APPENDIX 6

BIEXPONENTIAL MODEL

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The biexponential model is defined by the equation:

$$\text{ECD}_{\text{month}} = p \times e^{-a \times \text{month}} + q \times e^{-b \times \text{month}} + \varepsilon.$$

The model is used to fit the ECD pattern from baseline to 48 months after IMT implantation. For each eye at each visit, the average of all available ECD readings was used as the ECD measurement for the eye at that visit. ECD readings made after IMT explantation were not used since these readings were confounded by the removal of the IMT and implantation of a conventional IOL, however all available ECD readings made prior to IMT explantation were included in the model. The methods employed in the modeling were discussed with W. Bourne, M.D., Professor of Ophthalmology, Mayo Clinic, who was retained as a consultant to VisionCare on methods for analysis of endothelial cell loss. Dr. Bourne confirmed that the methods, as presented in this document, employed by VisionCare are appropriate.

The first term, $p \times e^{-a \times \text{month}}$, of the bi-exponential model represents the "rapid" rate of loss rate associated with the surgical trauma while the second term, $q \times e^{-b \times \text{month}}$, represents the "slow" rate of loss that occurs after stabilization. The quantity ε is an error term.

Having fit the model, the annual loss after stabilization is estimated as $(1 - e^{-b \times 12}) \times 100\%$. The predicted mean ECD at 3, 12, 24, 36, and 48 months and the corresponding 95% confidence intervals were calculated from the fitted model.

In addition to predicting mean ECD post-implantation, the probability that an individual eye would have ECD <1000, < 750 and <500 was predicted for various times after IMT-implantation using the empirical distribution of residuals as follows:

- For each observed ECD measurement, residual = observed ECD – predicted ECD.
- Since $(\text{observed ECD} < 1000) \cong (\text{residual} + \text{predicted ECD} < 1000) \cong (\text{residual} < 1000 - \text{predicted ECD})$, the probability of observed ECD at certain month <1000 is predicted by the proportion of residuals at the corresponding month less than 1000 minus the predicted ECD at the corresponding month.

Selection of the threshold limits of <1000 cells/mm², <750 cells/mm² and <500 cells/mm² in IMT-implanted eyes was based on a number of considerations, including age of the population indicated for IMT implantation, the probability of ECD falling below these limits over time, and existing clinical and regulatory precedent.



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IMPLANTABLE MINIATURE TELESCOPE (IMT™)
PMA P050034**

**PANEL PACKAGE FOR OPHTHALMIC DEVICES
ADVISORY PANEL MEETING MARCH 27, 2009**

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