

NEI and FDA Address the Use of Patient Reported Outcomes in Medical Product Development

On October 13, the NEI and the Food and Drug Administration (FDA) held the third of a series of ARVO-managed symposia about endpoints appropriate for use in clinical trials that support approvals for new drugs and devices. Entitled *Use of Patient-Reported Outcomes in Medical Product Development*, the meeting featured representatives from the reviewing divisions within FDA's Center for Drug Evaluation and Research (CDER) and the Center for Devices and Radiological Health (CDRH) that oversee ophthalmic drug and device approvals, respectively.

A Patient Reported Outcome (PRO) is a measurement of any aspect of health status that comes directly from the patient without having been interpreted by a physician or researcher. Because some treatment effects are known only to the patient, PROs are increasingly recognized as an essential component to be considered in the evaluation of drugs and medical devices. Quality of life indicators that arise from PROs are increasingly used in decisions about drug and device reimbursement, and are even being considered in potential health care reform legislation.

"Simply stated, this meeting will address

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Dr. Rohit Varma

how patients report their perception of vision in relation to clinical outcomes," stated NEI Director Paul Sieving, M.D., Ph.D., who noted the importance of these discussions within NIH. Symposium co-chairs Neil Bressler, M.D. (Wilmer Eye Institute/Johns Hopkins) and Rohit Varma, M.D. (Doheny Eye Institute/University of Southern California) emphasized the importance of PROs in vision trials and epidemiologic assessments sponsored by NEI and industry. At issue was whether a PRO could be used as a primary endpoint in new product evaluation and, if so, what would it take to develop and validate that PRO, similar to that which is done with clinical data. A corollary issue was the impact of PROs on product labeling claims or other patient information.

Since PROs are increasingly being con-

sidered in new product evaluations across the FDA, representatives of its Division of Epidemiology discussed concepts that are incorporated into a draft FDA guidance document entitled *Patient-Reported Outcomes Measures: Use in Medical Product Development to Support Labeling Claims*, which will issue shortly in final. They encouraged attendees to consider meeting early with the reviewing division to discuss the potential use of PROs in the regulatory submission.

CDER representative Wiley Chambers, M.D., (Acting Director, Division of Anti-Infective and Ophthalmic Products) commented that, for ophthalmic drug approval, there is no requirement for a quality of life study in addition to safety and effectiveness, but if a manufacturer wants to use a PRO in a label claim, then it must be developed and validated. CDRH representative Malvina Eydelman, M.D. (Director, Division of Ophthalmic, Neurological and Ear, Nose and Throat Devices) commented that, although PROs are not usually primary endpoints, they are considered in safety reviews of a device both pre- and post-market and may be included on separate information sheets to patients. She reported that FDA would announce a collaborative study

with the NEI that would use PROs to examine the potential impact on quality of life from Laser-Assisted In Situ Keratomileusis (LASIK), a form of laser eye surgery to improve vision. The study will identify factors that can affect quality of life following LASIK and potentially reduce the risks of adverse effects.

Anne Coleman, M.D. (Jules Stein Eye Institute/University of California-Los Angeles) identified challenges to the use of PROs in ophthalmic drug and device approvals, including developing appropriate measurements and validating these on an ongoing basis. Dr. Varma concluded by stating that, although the vision community may not yet be prepared to use PROs as primary endpoints, they serve an important current and future role in the evaluation of new treatments.



Left to right: *PRO Endpoints* Symposium co-chairs Neil Bressler, M.D. (Wilmer Eye Institute/Johns Hopkins) and Rohit Varma, M.D. (Doheny Eye Institute/University of Southern California)



Left to right: Malvina Eydelman, M.D. (FDA/CDRH, Director, Division of Ophthalmic, Neurological and Ear, Nose and Throat Devices) and Susan Vitale Ph.D. (NEI Division of Epidemiology and Clinical Applications)



Wiley Chambers, M.D., (FDA/CDER, Acting Director, Division of Anti-Infective and Ophthalmic Products)



Left to right: William Rich, III, M.D., F.A.C.S., representing the American Academy of Ophthalmology, NEI Director Paul Sieving, M.D., Ph.D., and Dr. Varma



Left to right: Anne Coleman, M.D. (Jules Stein Eye Institute/University of California-Los Angeles) and NEI's Clinical Director Rick Ferris, M.D.

The *PRO Endpoints* symposium was developed after a session on quality of life indicators at the second of the joint NEI/FDA meetings, *Glaucoma Clinical Drug Trial Design and Endpoints*, held in March 2008. The first symposium, *Ophthalmic Clinical Trial Design and Endpoints*, held in November 2006, focused on new treatments for AMD and diabetic retinopathy.