

## Will CXL Get Approval in 2014?

### *A leading researcher weighs in on crosslinking trials*

There are currently three corneal crosslinking (CXL) clinical trials in the FDA pipeline, and researchers hope the "original" US CXL trial, which began in 2008, will be approved in the United States in 2014. CXL uses ultraviolet light and riboflavin drops to form links between collagen molecules that strengthen the cornea and impede the progression of keratoconus (KC).

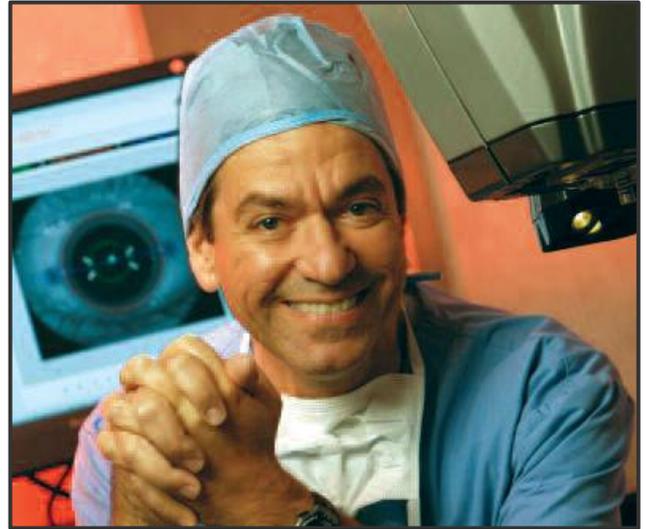
The first CXL trial, which was conducted in 10 sites with nearly 500 eyes treated, is in final stages of the FDA approval process. That trial began enrolling participants in 2008, and treatments were completed about two years later. Follow-ups were done with all patients for a year, before data was analyzed, reviewed and prepared for FDA review.

"All treatments have been done, the follow-up has been completed, the data analysis has been done, and it is currently in the approval process," says Dr. Peter Hersh, medical monitor of the crosslinking clinical trials,

director and founder of the Cornea and Laser Eye Institute – Hersh Vision Group in New Jersey, and director of the Cornea and Refractive Surgery Division at Rutgers New Jersey Medical School. "From my point of view, it meets all the expectations we want: It shows crosslinking is effective and a safe procedure for patients with keratoconus and, indeed, it is effective in diminishing the progression of keratoconus compared with patients who received placebo drops, so we know it is really working."

"From a medical viewpoint, there is no reason not to expect FDA approval," Hersh says. "The FDA has been actively involved and is aware of the need for the procedure. If all goes well, in terms of the approval process, I would hope it would be approved in the new year."

A second clinical trial using a new ultraviolet device for accelerated crosslinking was completed earlier this year. It uses higher power, so treatment can be completed in a shorter amount of time. This trial, which treated 220 eyes in a randomized trial



Dr. Peter Hersh is the medical monitor of the CXL trial under current review by the FDA.

comparing it with a placebo, is currently in the patient follow-up phase. Hersh and his colleagues are starting a third randomized crosslinking trial using pulsed CXL, which employs a noncontinuous beam of light. The reason for this study is CXL scientists have demonstrated that additional oxygen within the cornea during the procedure may lead to a greater crosslinking effect. "It's a whole new approach and a new modality," Hersh says. This trial will take place in 10 study sites and follow all guidelines for FDA approval.

There are also physician-sponsored CXL trials being conducted throughout the country; these trials aren't necessarily being done specifically for FDA approval, though they usually are done under strict regulatory oversight. One such trial is being conducted by the American-European Congress of Ophthalmic Surgery (ACOS) to look at using different UV powers during CXL. The ACOS trial is quite large — up to 4,000 subjects at 100 sites — and is looking at the efficacy of different UV powers on crosslinking results, Hersh says.

All CXL trials currently looking toward FDA approval use the "epi-off" technique of CXL, in which the epithelium is removed. Proponents of epi-off believe more crosslinking occurs if the riboflavin drops do not have to penetrate the epithelium. "Epi-on" crosslinking leaves the epithelium intact, which results in less healing time following the procedure.

"Is the amount of corneal crosslinking and the longevity of the crosslinking equivalent with epi-on? And if it's less, is it worth the advantage of a shorter healing time? That's the ultimate question," Hersh says.

If you'd like to help researchers find out the answer, look into physician sponsored clinical trials currently underway studying just that.

**For information about CXL clinical trials, visit [www.nkcf.org/clinical-trials](http://www.nkcf.org/clinical-trials).**

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