

# Waxler Regulatory Consultancy LLC

1920 Arlington Place  
Madison, WI 53726-4002

608-219-7547  
[mwaxler@charter.net](mailto:mwaxler@charter.net)

July 22, 2014

Nancy K. Slade, J.D.  
Division of Dockets Management  
Food and Drug Administration  
Department of Health and Human Services,  
Rm. 1-23  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852.

Re: Petition for Reconsideration [Docket No. FDA-2011-P-0022]

Dear Dr. Slade:

In accordance with 21 CFR 10.33 the undersigned submits this petition for reconsideration of the decision of the Commissioner of Food and Drugs in Docket No. FDA-2011-P-0022, issued in the June 23, 2014 letter from Nancy K. Slade, CDRH Deputy Director for Policy.

## A. Executive Summary

The agency letter agrees with the petitioner that FDA approved the PMAs for LASIK devices with adverse event rates of approximately 20%.<sup>1</sup> However, the agency declares the 20% values clinically insignificant even though it cites NO data. Finally, the agency uses a 1% rate that was NOT used as the basis for approval of any of the PMAs, saying that "... this figure generally reflects the experience of the majority of LASIK patients;" again without citing data from the PMA. The agency grossly underestimates the risks of LASIK by conflating data used to legally support the PMA orders with LASIK industry information used to promote sales.

FDA's denial of the petition sends two messages:

**LASIK Industry:** Feel secure - the agency has your back. The agency will not investigate or enforce laws against those who submit an PMA application that "... contained or was accompanied by an untrue statement of a material fact, section 515(e)(1)(C) of the FD&C Act." FDA will not investigate secret files, withholding of data in clinical trials, cherry picking, failing to report adverse events, or MEDWATCH reports.

**Public:** Beware - FDA does not have your back. The agency admits that LASIK has an adverse event rate of about 20%, falsely advertises it as 1% and, instead of *caveat emptor*, the agency promotes LASIK. Instead of requiring an epidemiological study of LASIK, the agency collaborates with the LASIK industry to persuade the public the satisfaction rate is high after LASIK. Consumers who file MEDWATCH reports of LASIK-injuries are ignored; FDA will not act on the reports for public safety."

The petitioner hereafter states the Decision Involved in reconsideration of FDA-2011-P-0022, the Actions Requested, and the Statement of Grounds for reconsideration. The Commissioner did not adequately consider the record of industry pressure on the agency, the MEDWATCH reports, other sources of adverse event data, and conflation of patient satisfaction information with adverse event data.

#### **B. Decision Involved**

The petitioner wishes the Commissioner to reconsider the agency's decision to deny the request of the petition for the withdrawal of PMAs for all LASIK excimer laser devices and for the issuance of a public health advisory with a voluntary recall of the devices.

#### **C. Action Requested**

The petitioner requests the Commissioner initiate the following action plan preparatory to a public health advisory and PMA withdrawals:

- 1) Cease promotion of LASIK on FDA's website. The agency knows the adverse event rate is approximately 20% and should stop implying that it is 1% without industry submission of PMA data supporting this claim. Also, FDA should highlight the *caveat emptor* language incorporated into the PMA approved labeling that was specifically designed for consumer protection.
- 2) Begin an investigation of LASIK industry regulation, including
  - i. Root cause analysis of LASIK adverse event data. Analysis should include all sources of data including but not limited to MEDWATCH files (>1,000 complaints), eyes treated while PMAs under review (>20,000 eyes?), unreported investigational studies (>100 studies, >20,000 eyes), and secret files maintained by user facilities and manufacturers (the petitioner is aware of one secret file).
  - ii. Seeking out and reviewing allegations by the petitioner and others that manufacturers and associated user facilities, investigators, organizations and individuals have withheld, manipulated, destroyed, and otherwise modified data and information submitted to the FDA in support of filings to the agency.
  - iii. Conduct an epidemiological study of the safety/effectiveness of LASIK using information from existing data sources and stratified by device use, date, condition, and other relevant parameters.

- iv. Investigate quality systems of LASIK manufacturers and user facilities with focus on complaint handling and corrective and preventive action.
- 3) Take regulatory actions as deemed appropriate, including but not limited to public health warnings and PMA withdrawals.

### C. Statement of Grounds

The grounds for reconsideration is based on the following specific and relevant information and views contained in the administrative record of FDA-2011-P-0022 that were not previously or not adequately considered by the Commissioner:

1. The agency letter denying FDA-2011-P-0022 clarifies the issue of adverse event rates.
  - a. FDA reviewers agree with the petitioner that the adverse event rates for dry eyes, night vision, glare, and halos are approximately 22%, 16%, 20%, and 19%, that is, “The rate of the adverse events reported in the literature cited in your petition appears to be consistent with the information provided in the PMA applications for the LASIK devices.,,”
  - b. However, FDA reviewers confounded the adverse event rate data in the PMA submissions with patient satisfaction data NOT in the PMA submissions:
    - i. The high rate (averaging 20%) adverse events (HRAEs) were reported in each PMA were, and are, inconvenient facts for FDA and the LASIK industry.<sup>2</sup>
    - ii. The LASIK industry claimed these problems (dry eyes, night driving problems and a few others) were clinically insignificant and less than or equal to 1% by 12 months post-LASIK. The data in the PMA, however, does NOT confirm this hypothesis. The agency fails to mention that the frequency of LASIK-induced dry eyes is so high and so long-lasting that sales of eye drops have sky-rocketed. Yet agency’s advertising continues to minimize the public health significance of this adverse event.
    - iii. The FDA / industry solution to the existence of HRAEs evolved as follows. It is interesting that the agency does not mention the extensive industry pressure on this matter:
      - a) *Caveat emptor* labeling was developed by FDA to cover the HRAEs that were found. The petitioner played a major role in crafting this labeling.
      - b) The LASIK-industry developed euphemisms for the HRAEs to minimize the negative connotation of “adverse events”, e.g. symptom, complication. The petitioner agreed with the Office Director’s view that the euphemisms could be used as subcategories of adverse events but that the HRAE percentages should be counted in the overall 1% criterion for PMA approval.
      - c) Industry proposed using global patient satisfaction measures instead of specifically identified adverse events, e.g. dry eyes. The petitioner was part of the early negotiations on developing quality of life measures of

patient satisfaction but relinquished these responsibilities to the Director of the Division of Ophthalmic Devices.

- d) HRAE percentages were excluded from calculation of the overall percentage target adverse event needed for PMA approval. The PMAs were approved based only on the low rate adverse events (<1%), such as loss of visual acuity, induced astigmatism and corneal ectasia. The petitioner is not aware of when and how this happened. This is a key question for investigators.
  - e) FDA minimizes reference to HRAE percentages where ever possible in public communications. This practice appears to have begun after the petitioner left leadership of the Diagnostic and Surgical Devices Branch.
  - f) In public communications FDA conflates percentages derived from “patient satisfaction” data with those based on “adverse event” data. This practice appears to have begun with launch of the LASIK webpage and continues.<sup>3</sup>
- c. The agency deleted Figure 1 from its LASIK webpage but says the figure correctly shows minimal symptoms post-LASIK as “...generally reflecting the experience of the majority of LASIK patients”.
- i) What is the source data for this figure?
  - ii) Did industry prepare this figure or not?
  - iii) Was this data submitted to FDA in a premarket application or an investigational device exemption?
  - iv) Why does this data differ so dramatically from that available in the PMAs?
  - v) Where in the PMA process, and for which manufacturers, did the agency supplant the tables on the 12 month adverse events at approximately 20% of dry eyes, night vision problems, glare, and halos with Figure 1 showing rates <1%?
  - vi) Why did FDA delete Figure 1 from its website if the data accurately, reliably, and validly represents the experience of most LASIK patients?
  - vii) What is FDA’s scientific rationale for preferring industry Figure 1 (<1%) as an estimate of post-LASIK adverse events than the ones obtained in each of the PMA studies (>20%)?
2. The agency letter denying FDA-2011-P-0022 did not discuss the effects of the relentless pressure of the industry in effectively neutering public health actions by FDA vis-a-vis LASIK adverse events. In an attempt to bring the LASIK industry under regulatory control, the FDA made deals<sup>4</sup> with the following industry entities that degraded the scientific quality of the collection and analysis of adverse event data of LASIK devices:

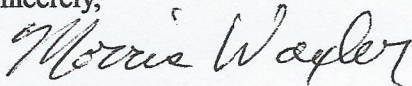
- a. Kremer Laser - Agreement to accept data in a PMA submission in lieu of prosecution for violations of multiple FDA regulations. FDA approved P970005 after panel recommended disapproval.
  - b. American Society for Cataract and Refractive Surgery - Agreement not to prosecute user facilities for performing off-label LASIK if the facilities submit investigational device exemptions;
  - c. CRS Inc - Agreement to conduct large LASIK clinical studies for submission of PMAs to be purchased by VISX and Summit. The trials would use a referral system for trial management and the collection of adverse event data.
  - d. More than one hundred user facilities - Each facility received investigational device exemptions to study LASIK in order to minimize their exposure to violating off-label rules.
3. The agency letter denies issuance of a Public Health Warning even though it has NOT provided analyses of LASIK complaint and adverse event files available to it. Therefore, FDA is preventing an objective assessment of the risks associated with LASIK and blocking corrective and preventive actions, including a Public Health Warning and enforcement actions:
- a. The agency provides no information on how many MEDWATCH reports it has analyzed, what conclusions have been reached, and what actions have been taken; all the while asserting it conducts a "...continued assessment of... medical device reports...".
  - b. The agency provides no information about patient complaint files and correction and preventive actions at LASIK facilities where the Office of Compliance has issued Warning Letters. What are the adverse event rates at the facilities? Which of these facilities have secret complaint and adverse event files? When did the manufacturers of the LASIK devices distributed to these facilities become aware of the secret files?<sup>5</sup>
  - c. The agency did not provide analyses of the adverse event rates in the more than 20,000 eyes that received LASIK. These data exist in FDA files.
4. The agency letter denying FDA-2011-P-0022 is anti-consumer, pro-industry:
- a. The agency ignores thousands of MEDWATCH reports of LASIK injuries while promising otherwise:<sup>6</sup>
  - b. FDA prevents access of prospective LASIK patients to PMA-approved patient information pamphlets, meanwhile touting its availability.<sup>7</sup>
  - c. FDA characterizes LASIK-induced progressive pathological changes in the corneal as healthy and known at the time of PMA approvals. They are neither. FDA has evidence that LASIK creates "sick" corneas, doesn't know how sick the corneas are or will become, thinks that is just fine and has no proactive public health plan to deal with the consequences.

July 22, 2014

- d. The agency minimizes the potential importance of the progressive corneal pathology by calling them "... physiological changes... FDA believes that it is adverse medical events, and not physiological changes, that are important in determining whether LASIK devices are reasonably safe and effective. For example, even assuming that there is reduced density of corneal stromal keratocytes in post-LASIK patients, this may not lead to an adverse event. As you noted in your petition, the reported incidence of keratectasia in the cited literature ranges from 0.01% to 0.66%." The agency fails to mention the sight threatening and painful consequences of keratectasia. Moreover, the agency fails to mention that the LASIK industry is making a considerable effort to obtain FDA approval of drugs to cross-link the corneas of LASIK patients to prevent this sight-threatening problem. The petitioner has reviewed files of LASIK facilities where reports of keratectasia are hidden and has heard audio recordings of refractive surgery meetings which suggest the rate of keratectasia is much higher than that reported in clinical literature.
- e. The agency claims that the petitioner "...did not provide information in your petition to support your allegation...[that] LASIK device manufacturers withheld an average of about 30% of the clinical follow-up data (including instances of dry eyes, night vision problems, glare, and halos) from FDA."
  - i. The petitioner provided Tables 1 and 1A specifying the relevant data tables in the PMA documents. On what grounds does FDA deny the evidence presented in Tables 1 and 1A?
  - ii. What else do the numbers in the column labeled "% Data Withheld" represent? Has the agency audited the source data for these tables?

The petitioner requests reconsideration of FDA-2011-P-0022 because the Commissioner did not adequately consider the record of prolonged industry pressure on the agency nor use data available to the agency to determine if the adverse event rate is higher than 20%. I urge FDA to cease promotion of LASIK, investigate LASIK industry regulation, and take regulatory actions as deemed appropriate, including but not limited to public health warnings and PMA withdrawals.

Sincerely,



Morris Waxler, Ph.D.

President

<sup>1</sup> p.6 referring to Table 2 of the petition - "... The rate of the adverse events reported in the literature cited in your petition appears to be consistent with the information provided in the PMA applications for the LASIK devices..."

<sup>2</sup>The agency's letter criticizes the petitioner for providing an invalid summary of the data without providing one of its own, instead dismissing the HRAE data as NOT clinically significant.

<sup>3</sup>The agency praises a quality of life study designed to validate the use of the LASIK industry's 1% patient satisfaction rate. The study was completed in February 2014 with no data reported as of July 2014. The agency/industry has been using the 1% rate for years without validation to minimize the 20% adverse event rate reported in the PMA.

<sup>4</sup> After retirement from the FDA, the petitioner received an award with the following inscription: "CRS-IRS Award For Outstanding Contribution To The Research & Development Of Refractive Surgery Awarded To Morris Waxler, Ph.D. In Grateful Appreciation For His Years Of Dedication And Service To The Advancement Of Refractive Surgery We Are Extremely Grateful For Your Contributions To The Field Of Ophthalmology J. Charles Casebeer, MD., Guy M. Kezirian, MD. FACS, David J. Shanzlin, MD ISRS Fall World Refractive Surgery Symposium, Dallas, Texas Awarded This 20th Day Of October 2000"

<sup>5</sup> For example, the petitioner has reviewed a secret file of hundreds of injuries at LASIK facilities.

<sup>6</sup> "...if a patient has persistent, visual symptoms, then these symptoms should be reported and FDA will conduct an evaluation of those symptoms (<http://www.eyeworld.org/article-fda-interest-in-lasik-continues--ascrs-webinar-clears-confusion-about-medical-device-reporting-and-lasik>).” That under 21 CFR Part 803 it "... encourages such reporting so that the Agency may continue to assess relevant safety information on LASIK devices as part of its postmarket surveillance program.”

<sup>7</sup> "... the risks associated with each LASIK device are described in the patient labeling, and FDA's LASIK website provides information about the devices and the procedure, including a summary of the most common risks and links to the Summary of Safety and Effectiveness Data (SSED) and patient labeling for each approved LASIK device.”