MDDT Summary of Evidence and Basis of Qualification Decision for Patient-Reported Outcomes with LASIK (PROWL) Version 1.0.

Background

MDDT Name: Patient-Reported Outcomes with LASIK Symptoms and Satisfaction (PROWL-SS)

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Tool Description and Principle of Operation

The PROWL-SS scales are a set of items developed in response to patient concerns with outcomes related to Laser-Assisted *In Situ* Keratomileusis (LASIK) procedures. Included in the PROWL-SS are the visual symptoms and satisfaction with vision scales. The Visual Symptoms scales include items assessing the existence, bothersomeness, and impact on usual activities in the last 7 days of four key visual symptoms: double images, glare, halos, and starburst. Each item uses polytomous response options, and single scale score results for each symptom. These items are administered using a written definition of the symptom and photographic images to illustrate various levels of symptom severity to minimize confusion related to visual symptom terminology. The Satisfaction with Vision item is a single polytomous response item assessing the patient's satisfaction with his or her current vision.

Qualified Context of Use

The paper and electronic versions of the PROWL-SS visual symptom and satisfaction with vision scales can be used to assess the existence, bothersomeness and impact on usual activities in the last 7 days of four visual symptoms – double images (8 items), glare (8 items), halos (8 items), and starbursts (8 items) – as well as satisfaction with vision (1 item), in patients undergoing LASIK surgery who meet the following conditions: 21 and older who speak and read English fluently; have not previously received any form of refractive surgery; are determined to be good candidates for LASIK based on their surgeon's assessment of medical and ophthalmic health, cognitive function, and physical function and social function; are undergoing the surgery for treatment of myopia, hyperopia and/or astigmatism; and are targeted to get a refraction of bilateral emmetropia or slight hyperopia (+0.25 diopters). The four symptom scores may be used at baseline and post-surgery as a secondary or additional safety endpoint in clinical

studies or observational studies to evaluate descriptively the subjects' visual perception. The satisfaction with vision scale may be used at baseline and post-surgery as an additional effectiveness endpoint to evaluate descriptively changes in satisfaction from baseline.

SUMMARY OF EVIDENCE TO SUPPORT QUALIFICATION

The transcripts from the April 25, 2008 FDA Ophthalmic Device Panel 110th Meeting[1], the published results of the PROWL-1 and -2 studies[2,3], and summaries from additional qualitative studies were submitted to support the qualified context of use. The public meeting transcripts[1] highlight the importance of the content to patients, while the summaries of other qualitative work demonstrated the items were adjusted to ensure patient understanding. The PROWL-1 and -2 studies[2,3]provide quantitative evidence to support the use and interpretation of the PROWL Version 1.0 scales. The version of the PROWL questionnaire used in the PROWL-1 and PROWL-2 studies[2,3], referenced in the publications, and available on the National Institutes of Health (NIH) website[4] includes additional items, scales, and questionnaires that were not subject to Medical Device Development Tools (MDDT) review. Inclusion of these additional items, scales, or questionnaires should be discussed with FDA prior to initiating a study. The evidence submitted supports the validity and reliability of the PROWL Version 1.0 for use in LASIK device clinical studies, consistent with the COU. The evidence to support the PROWL-SS scales is summarized as follows:

Reliability

The reliability of the symptom scales was supported using a Cronbach's Alpha, a measure of internal consistency, and test-retest reliability. Only test-retest reliability was available for the satisfaction with vision scale, as it consists of a single item. Cronbach's Alpha was consistently high for all symptom scales across both PROWL studies, ranging from 0.95 to 0.98. Test-retest reliability was assessed with the second assessment administered with a mean follow-up of 10.74 and 6.34 days for PROWL-1 and PROWL-2, respectively. A summary of the test-retest results is presented in Table 1, intraclass correlations coefficients (ICC) generally range from acceptable to good.

Table 1. Test-Retest Reliability of the PROWL scales

Scale	Test-Retest (ICC)
Glare, 8 items	
PROWL-1	0.60
PROWL-2	0.66
Starburst, 8 items	
PROWL-1	0.80
PROWL-2	0.66
Halos, 8 items	
PROWL-1	0.78
PROWL-2	0.75
Double Images, 8 items	
PROWL-1	0.49
PROWL-2	0.88
Satisfaction with Vision, 1 item	
PROWL-1	0.69
PROWL-2	0.67

Validity Evidence Based on Content

The April 25, 2008 FDA Ophthalmic Devices Panel 110th meeting[1] provided the motivation for the PROWL studies and the foundation for the content included in the PROWL-SS scales. The symptoms and aspects of symptoms identified by patients and clinicians, for which no scale or items existed, were used as the basis for the items in the PROWL-SS symptom scales. Satisfaction with current vision was also identified as important to patients following the LASIK procedure. The reports from additional interviews conducted were submitted to demonstrate that changes were made to items to ensure patients understood the items as intended. Photographic images were included in the scales to help ensure patients interpret the visual symptoms in a consistent manner.

Validity Evidence Based on the Construct

The results of the PROWL-1 and PROWL-2 studies[2,3] were submitted to provide validity evidence based on the construct. The studies provided longitudinal data to support the responsiveness of the PROWL-SS. Pre-operative scores were compared to scores at 1, 3, and 6 months post-operative, presented in Table 2. Item level results for the symptom scales also provided evidence of the validity of the scale scores.

Table 2: Baseline and Post-Operative Scale MeansScale	Pre-Op Mean	1-Month Post-Op	3-Month Post-Op	6-Month Post-Op
Glare, 8 items				
PROWL-1	80.7	83.9	90.0	92.7
PROWL-2	81.2	86.2	88.6	--
Starburst, 8 items				
PROWL-1	74.5	78.6	84.3	86.3
PROWL-2	69.9	72.7	79.6	--
Halos, 8 items				
PROWL-1	79.0	76.3	84.3	88.1
PROWL-2	73.9	69.9	80.0	--
Double Images, 8 items				
PROWL-1	87.3	96.3	97.2	97.2
PROWL-2	85.3	95.0	97.4	--
Satisfaction with Vision, 1 item				
PROWL-1	36.2	89.1	90.9	91.5
PROWL-2	44.4	84.7	87.3	--

Evidence of the relationship between satisfaction with vision and visual symptom scores are presented in Table 3 using correlations. The positive correlations, while small to moderate, indicated that higher satisfaction was generally associated with higher (better) visual symptom scores, as expected. Additionally, the relationships between dry eye symptom severity, as categorized by the Ocular Surface Disease Index (OSDI), and the PROWL Version 1.0 scale scores were presented, with more severe dry eye symptoms associated with lower scores for both the individual symptom scores and satisfaction. The distribution of satisfaction with vision at each time point also indicated that the satisfaction with vision scale captures varying levels of improvement in satisfaction after surgery.

Table 3. Correlations of Satisfaction Scores with Visual Symptom Scores

	3-Months		6-months
Symptom	PROWL-1	PROWL-2	PROWL-1
Double Images	0.27	0.24	0.34
Glare	0.29	0.26	0.33
Halos	0.35	0.33	0.43
Starbursts	0.26	0.34	0.34

DISCUSSION OF THE EVIDENCE STRENGTH TO SUPPORT QUALIFICATION

Two major sources of evidence were used to support the qualification of the PROWL-SS. The transcripts for the FDA Ophthalmic Device Panel Meeting[1] provided a strong basis for the public health need to better measure outcomes in LASIK procedures. Additionally, these transcripts provide a basis for identifying the appropriate content to be measured by the scales. The PROWL-1 and PROWL-2 studies[2,3] provided quantitative evidence from large samples of patients who have undergone LASIK

surgery. The current evidence demonstrates adequate reliability of the scores to describe the symptom experience of patients undergoing LASIK surgery. The change of the symptom and satisfaction scores across time, as well as the relationships with other outcomes adequately support the validity of the scores within the approved context of use.

ASSESSMENT OF ADVANTAGES/DISADVANTAGES OF QUALIFICATION

Assessments of Advantages of Using the MDDT

The primary advantage of the MDDT is that is provides a reasonably reproducible quantification of the existence, bothersomeness, and impact on usual activities of 4 visual symptoms that may result from the LASIK procedure. As documented in the public meeting[1], the risk of visual symptoms can be a concern for patients considering LASIK surgery. The PROWL-SS Visual Symptom scales can help quantify and provide patients and clinicians with information regarding the visual symptoms. The satisfaction with vision scale provides a simple assessment of satisfaction with the results of treatment, which can also help inform future patients about the possible subjective assessment of the results of the procedure.

Assessments of the Disadvantages of Using the MDDT

The following disadvantages of using the MDDT were identified: 1) Inability to measure all of the important concepts related to the possible outcomes of LASIK surgery and 2) insufficient evidence to determine a clinically meaningful difference or score estimate. The inability to measure all important possible outcomes from LASIK surgery can be mitigated through the use of the symptom scales as a secondary or additional safety endpoint and the use of other existing assessments to address other relevant patient-reported outcomes. For instance, some assessments used in the PROWL-1 and PROWL-2 studies[2,3], such as an assessment of the symptoms and impact of dry eye or driving difficulty, may be fit-for-purpose and could be useful additions. The lack of evidence to aid in the interpretation of scores will be mitigated as more studies using the PROWL-SS scales are published and can currently be mitigated by presenting the PROWL-SS scales using descriptive statistics.

CONCLUSIONS

The importance of the content to patients and clinicians, as well as the additional qualitative work and the results of the PROWL-1 and PROWL-2 studies[2,3] provide sufficient evidence to support the validity and reliability of the PROWL-SS in the qualified context of use.

CONTACT INFORMATION FOR ACCESS TO TOOL

For access to the PROWL-SS, please contact:

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REFERENCES

1 CDRH Advisory Meeting Materials Archive. http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfAdvisory/details.cfm?mtg=695.

2 Hays RD, Tarver ME, Spritzer KL, et al. Assessment of the Psychometric Properties of a Questionnaire Assessing Patient-Reported Outcomes With Laser In Situ Keratomileusis (PROWL). JAMA Ophthalmology 2017;135:3-12.

3 Eydelman M, Hilmantel G, Tarver ME, et al. Symptoms and Satisfaction of Patients in the Patient-Reported Outcomes With Laser In Situ Keratomileusis (PROWL) Studies. JAMA Ophthalmology 2017;135:13-22.

4 National Institutes of Health Common Data Elements Repository: Patient-Reported Outcomes with LASIK (PROWL) Pre/Post-Operative Questionnaire.

https://cde.nlm.nih.gov/form/search?selectedOrg=NEI&classification=LASIK%20Quality%20of%20Life%20Collaboration%20Project