DE NOVO CLASSIFICATION REQUEST FOR NOTAL VISION HOME OPTICAL COHERENCE TOMOGRAPHY (OCT) SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Home monitoring ophthalmic imaging device.** A home monitoring ophthalmic imaging device is a prescription self-imaging device that incorporates imaging system hardware and automated image processing and analysis to enable patients at home to provide measurements that are intended for use by a physician for monitoring ophthalmic diseases or conditions in between regularly scheduled assessments.

NEW REGULATION NUMBER: 21 CFR 886.1600

CLASSIFICATION: Class II

PRODUCT CODE: SAX

BACKGROUND

DEVICE NAME: Notal Vision Home Optical Coherence Tomography (OCT) System

SUBMISSION NUMBER: DEN230043

DATE DE NOVO RECEIVED: June 7, 2023

SPONSOR INFORMATION:

Notal Vision, Inc.
7717 Coppermine Drive
Manassas, VA 20109

INDICATIONS FOR USE

The Notal Vision Home Optical Coherence Tomography (OCT) System is indicated as follows:

> The Notal Vision Home Optical Coherence Tomography (OCT) System is an Artificial Intelligence (AI)-based Home Use device indicated for visualization of intraretinal and subretinal hypo-reflective spaces in a 10 by 10-degrees area centered on the point of fixation of eyes diagnosed with neovascular age-related macular degeneration (NV-AMD). In addition, it provides segmentation and an estimation of the volume of hypo-reflective spaces. The Notal Home OCT device is intended for imaging at home between regularly scheduled clinic assessments and not intended to be used to make treatment decisions or replace standard-of care regularly scheduled examinations and clinical

testing as needed, including in-office imaging and assessments for changes in vision, by an ophthalmologist.

LIMITATIONS

The sale, distribution, and use of the Notal Vision Home Optical Coherence Tomography (NVHO) System are restricted to prescription use in accordance with 21 CFR 801.109.

The Notal Home OCT System and Web Viewer results should not be used for diagnosis of any condition.

The NVHO device should not be used to delay in-office follow-up or to prolong the interim period between in-office follow-up visits.

The NVHO device should not be used on patients with nonneovascular AMD ("dry" AMD) to detect conversion from "dry" to "wet" AMD.

Patients should continue self-monitoring for visual changes (e.g., continue self-administration of Amsler grid testing) while using the NVHO device.

The Notal Home OCT device shall not be used by patients with Visual Acuity of worse than 20/320.

Scans with poor image quality, e.g., below Manufacturer Signal quality Index (MSI) of <2, may be unreliable. MSI values with color indicator are presented under the Web Viewer OCT B-scans. The following conditions may increase the likelihood of poor-quality scans:

- Inability to maintain steady fixation
- Unclear ocular media
- Dementia

NOA estimations should be considered in the context of the variability observed across the range of estimations (i.e. larger percent variability for NOA quantification of smaller hypo-reflective spaces); lower notification thresholds in the presence of smaller hypo-reflective spaces will be inherently less reliable.

Data on the clinical performance of Notal Home OCT System was limited in the following populations:

- Patients with vision worse than 20/80
- Patients of African and Asian descent and Hispanic/Latino patients

Caution should be exercised when evaluating scans from these patient populations. In addition, the ability of patients with vision worse than 20/80 to successfully self-image and to generate consistently reliable images with the Notal Home OCT System is not well characterized. Participants of the "006" clinical study comprised 21.5% of the safety cohort but 40.3% of those who failed to successfully self-calibrate.
Regular and frequent review of all available B-scans, regardless of TRO level, is recommended to evaluate for appropriate scan centration and quality, for the presence of confounding pathologies, and for the presence of hypo-reflective spaces abutting or spanning the edge of the scan area. Regular review of B-scans is also recommended to evaluate for hyper-reflective lesions such as hemorrhage. It is recommended to review and consider the information available over several (at least three) days in the trajectory. No single NOA estimation should be relied upon in making decisions about prompt patient follow-up.

Please refer to the "Notal Home Optical Coherence Tomography Instructions for Use" and "Notal Home OCT Web Viewer Instructions for Use" for a complete list of WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS, as well as a description of CLINICAL STUDY OUTCOMES ("Notal Home OCT Web Viewer Instructions for Use" only).

DEVICE DESCRIPTION

The NVHO System is a device that consists of two elements:

- **Notal Home OCT device**: patients use this to self-image their eyes using Spectral-Domain OCT; At the end of each scanning session the data is transmitted via a secured wireless communication to the Notal Health Cloud.
- **Notal Health Cloud**: cluster of servers and analysis units on which the Notal OCT Analyzer (NOA) analyzes the scans received from the Notal Home OCT device. Processed data are presented on a dedicated interactive web-application, the Notal Home OCT Web Viewer.

Figure 1: Notal Home OCT Device

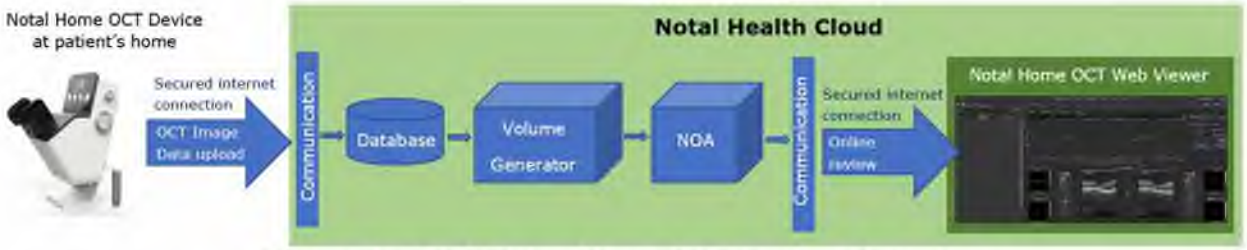

Figure 2: Notal Vision Home OCT System Overview

The system overview in Figure 2 shows the overall workflow. Images are captured by the patient at home. An application icon-based Graphical User Interface (GUI) enables NV-AMD patients to self-image. The GUI, presented on an external touch screen, takes the patient step-by-step through the scanning flow. The device contains an internal mini-display that presents an interactive fixation target to the subject. Upon self-imaging, images are automatically and securely transmitted to the Notal Health Cloud for viewing by the prescribing user. Raw data are fed into a Volume Generator (VG) module for OCT B-scan reconstruction, Manufacturer Signal Quality Index (MSI) calculation, segmentation, registration, volume scan reconstruction and alignment. Images are fed into the Notal Home OCT Web-viewer for display, and into NOA for analysis.

NOA is an artificial intelligence (AI) algorithmic module. NOA runs on the Notal Health Cloud and processes the volume scans generated by the VG. Its purpose is to segment the subretinal hypo-reflective spaces (SRO) and intraretinal hypo-reflective spaces (IRO) in the 2D B-scans. From this, the IRO and SRO volumes in the macular volume scan are calculated.

Total retinal hypo-reflective space (TRO) volume information, which is the sum of SRO and IRO, is displayed on the Notal Home OCT Web Viewer, NOA tab (see Figure 4), along with projections of SRO and IRO information. The Notal Home OCT Web Viewer and OCT images are not accessible to patient users.

Figure 3: Patient Using the Notal Home OCT Device

1. Hypo-reflective Spaces Volume Trajectories	2. NOA Movies	3. Timeline	4. Event Indicators
5. Hypo-reflective Spaces Thickness Maps	6. Scan Player	7. AI Segmentation Overlay	8. Manufacturer Signal Quality Index (MSI)
9. B- Scan	10. Lock Images	11. Present Time Points	12. Date Selector(s)
13. Time Range Display	14. Export Button		

Figure 4: Eyecare Provider's Interactive Viewer

Figure 4 shows the Notal Home OCT Web Viewer NOA tab display, which includes an output of TRO volume over time, along with projections and B-scan overlay. An image quality indicator, Manufacturer Signal quality Index (MSI) is displayed, with acceptable scan quality of MSI ≥ 2 indicated by a green color and an unacceptable scan quality MSI < 2 indicated in red. The prescribing user can compare two scans from two different dates, side-by-side. Prescribing-user set notifications are available, based on two notification categories (multi-selection is allowed):

1. TRO – if TRO reaches the threshold, a notification is generated
2. Time – if the selected number of days has elapsed, a notification is generated

Table 1: Notal Home OCT System Technical Specifications

Design Configuration	Notal Home OCT Device
Methodology	Spectral Domain OCT
Field of view	10°X10° measured from the cornea surface
Scan speed	10,000 A-scans / sec
Lateral number of pixels	500 A-scans / B-scan
Light source	Super luminescent diode (SLD)
Center wavelength	830 ± 10 nm
Optical resolution	Better than Axial 19 µm (in tissue), transverse 35 µm (in tissue)
Capture rate	Max: 20 B-scan/sec
Scan pattern	88 B-scans over the scanned area of 10°X10°
Maximal power on the cornea	710 µW
Maximal daily exposure	120 sec
Shut off optical power	800 µW
Spectrometer Specifications	
Number of pixels in image plane	512
Digital resolution (in tissue)	Better than 4.5 µm (in tissue)
Performance Measure	
Sensitivity (in air)	>100 dB
Electrical	
Voltage range	110-240 V
Frequency range	50-60 Hz
Power consumption	Up to 100 Watts
Power supply	90W single output external power medical grade, E-Cap Life of >7 years
Computer/OS	IMX6 quad core/Linux embedded
Input device	External touch screen
External screen	LCD 7"

Summary of Nonclinical/Bench Studies

Non-clinical testing for the NVHO device included device benchtop performance testing, optical radiation safety, software and cybersecurity, electromagnetic compatibility (EMC) testing, wireless testing, electrical safety testing, biological safety evaluation, and human factors validation testing.

Bench Performance Testing

Non-clinical performance testing was conducted to verify the technical specifications, spatial characteristics, device sensitivity and diopter range for the NVHO device on three identical devices.

Table 2: Verification of NVHO bench performance

Test	Purpose	Method	Acceptance Criteria	Results
Optical Coherence Tomography Bench Performance Verification				
Axial resolution	To verify axial resolution	(b)(4)		Passed

		(b)(4)	
Lateral resolution	To verify lateral resolution		Passed
Axial range	To verify axial range and axial distance calibration		Passed
Lateral range	To verify the lateral range and lateral distance calibration for each scan pattern		Passed
Device sensitivity testing	To characterize instrument signal-to-noise ratio (SNR) and instrument depth attenuation		Passed
Diopter range	To measure the device diopter range for compensating for refractive error of the patient.		Passed

OPTICAL RADIATION SAFETY

Optical radiation safety testing was provided to ensure the NVHO device provides acceptable light hazard protection, in accordance with the applicable parts of the following standard:

- ANSI Z80.36:2021: American National Standard for Ophthalmics – Light hazard protection for ophthalmic instruments

The test report for ANSI Z80.36:2021 included descriptions of all the light sources and their optical paths along with functions and technical specifications of these light sources. Measurement procedures, equipment used for measurements, raw data and formulas used for calculations were provided and were found to be acceptable. A justification was provided to explain why the worst-case scenarios were considered in the assessment of optical radiation safety.

SOFTWARE & CYBERSECURITY

The NVHO system is a cyber device per 524B(c) of the Food, Drug & Cosmetic Act. Notal Vision has followed the recommendations in the Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions (fda.gov) (https://www.fda.gov/media/119933/download) guidance document (September 27, 2023).

The NVHO System is comprised of the Notal Vision Home OCT device and the Notal Health Cloud. The device allows the patients to self-image their eyes, and have images securely transmitted from the device to the Notal Health Cloud. The images are then reconstructed on the cloud and made available to the patient's health care provider.

A detailed description of all software inputs and outputs was provided, along with description of all software modules and interactions with device hardware. All components of the device are controlled/monitored by software, which is responsible for the functionality, user interface, hardware start-up checks, and head position, pupil detection performance accuracy. A detailed description of data used to train and test the algorithms was provided, including cases, sources, demographics and reference standards. The software was developed and tested according to the following FDA guidance documents and recognized consensus standards:

- FDA Guidance, General Principles of Software Validation (January 11, 2002)
- FDA Guidance, Off-the-Shelf Software Use in Medical Devices (September 27, 2019)
- FDA Guidance, Guidance for the Content of Premarket Submission for Software Contained in Medical Devices (May 11, 2005)
- IEC 62304: 2006 /A1:2016 Medical device software - Software life-cycle processes
- ISO 14971:2019 Medical devices - Application of risk management to medical devices

Software documentation and testing, including cybersecurity information, demonstrates that the software will operate in a manner described in the specifications. The hazard analysis characterized software and cybersecurity risks, including device malfunction, measurement-related errors, head/pupil position sensors, power/internet/network connectivity and other hardware failures, and unauthorized access by malicious end users. The submission describes verification and validation testing to address the potential hazards with satisfactory results. The cybersecurity documentation included a cybersecurity hazard analysis and mitigation information, an upgrade and maintenance plan, other information for safeguarding the device during manufacturing and upon commercial distribution, and warning and precaution information in the product labeling.

Overall, the software documentation contains sufficient detail to provide reasonable assurance that the software will operate in a manner described in the specifications. Software security information demonstrated the device is protected from cyber vulnerability threats. All testing and results were considered to be adequate and met the above standards.

ELECTROMAGNETIC COMPATIBILITY, WIRELESS COEXISTENCE AND ELECTRICAL SAFETY

Electrical Safety and Electromagnetic Compatibility (EMC) testing has been performed as per the following recognized consensus standards and the results support electrical safety and electromagnetic compatibility

- IEC 60601-1: 2005, A1:2012, A2: 2020 Medical electrical equipment – Part 1: General requirements for basic safety and essential performance, including US National Deviations.
- IEC 60601-1-11:2015AMD1:2020: Medical electrical equipment – Part 1-11: General requirements for basic safety and essential performance-Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment.
- IEC 60601-1-2:2020: Medical electrical equipment-Part 1-2: General requirements for basic safety and essential performance-Collateral standard: Electromagnetic disturbances-Requirements and tests

BIOCOMPATIBILITY/MATERIALS

The NVHO includes five components that are in contact with intact skin: an enclosure (polyurethane), face rest (polyurethane (b)(4)), handles (thermoplastic polymer), touch screen (silicone dioxide) and volume and height control (polyurethane). A biocompatibility evaluation for each of the five patient-contacting components was conducted according to International Standard Organization (ISO) 10993-1:2018 *Biological evaluation of medical devices-Part 1: Evaluation and testing within a risk management process* and following FDA Guidance: Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" - Guidance for Industry and Food and Drug Administration Staff (fda.gov). This evaluation was found to be acceptable.

HUMAN FACTORS VALIDATION TESTING

Two Human Factors Summative Studies were conducted following the FDA guidance: "Applying Human Factors and Usability Engineering to Medical Devices" to evaluate the usability of the Notal Home OCT device and the Notal Home OCT Web Viewer.

A NVHO Human Factors Validation Study was conducted for subjects with NV-AMD and their caregivers to establish that the NVHO System patient user interface (NVHO device, and associated labeling) was safe and effective for intended users, uses and use environments by showing that use-related hazards associated with the NVHO System have been adequately

mitigated and instructional information for the user (Instructions for User, Packaging Set-up instructions) can be used effectively by representative users under simulated use conditions without producing patterns that could result in harm to patients, caregivers or providers. A total of 54 individuals representing two distinct user groups participated in this human factors validation test; 20 individual patients and 17 pairs of patient and caregivers (34 individuals). Patients went through a built-in, on-screen tutorial session, which provided training on how to self-image; this was provided along with on-package setup instructions and instructions for use. Critical tasks were identified that were related to the use of NVHO device. The testing determined that the Notal Home OCT patient interface and its associated labeling and packaging components are safe and effective for the intended user population in their intended use environment. Human factors validation testing did not yield any results that indicate use errors or patterns of use errors that could result in user harm. No use errors were observed on critical tasks, therefore, the results of the study demonstrate that the device user-interface supports the use-safety and effectiveness of use for the intended use. No additional modifications to the user interface were needed to lower the residual risk of the user interface.

A second Human Factors Validation Study was conducted for eyecare providers to establish that the NVHO System physician user interface (Web Viewer and associated labeling) was safe and effective for intended users, uses and use environments by showing that use-related hazards associated with the Notal Home OCT Web Viewer have been adequately mitigated and that instructional information for the user (user manual) can be used effectively by representative users under simulated use conditions without producing patterns of failures that could result in harm to users. A total of 15 eyecare providers participated in the human factors testing for the OCT Web Viewer. Critical tasks were identified that were related to reviewing of patient scans and use of features in the Web Viewer. The testing determined that the Notal Home OCT Web Viewer and its associated labeling are safe and effective for the intended user population in their intended use environment. Human factors validation testing did not yield any results that indicate use errors or patterns of use errors that could result in user harm. No use errors were observed on critical tasks, therefore, the results of the study demonstrate that the device user-interface supports the use-safety and effectiveness of use for the intended use. No additional modifications to the user interface were needed to lower the residual risk of the user interface.

SUMMARY OF CLINICAL INFORMATION

Clinical performance data were collected from two pivotal clinical studies: 1) the C2021.001 study ("001 Study"): A 5-Week "Home OCT Fluid Visualization Agreement Study"; 2) the C2012.006 study ("006 Study"): A cross-sectional in-office study for "The Evaluation of the Agreement and Precision of the Notal Vision Home OCT in the Automatic Fluid Quantification in Patients with NV-AMD."

Note: The protocols for these studies used the term "retinal fluid" (e.g., total, sub-retinal and intra-retinal fluid [TRF, SRF, IRF]) to refer to hypo-reflective spaces (HRS; or TRO, SRO, and IRO). However, not all hypo-reflective spaces on macular OCT imaging are retinal fluid, and not all exudative fluids will necessarily be hypo-reflective; therefore, the terms TRF, SRF, and IRF are not synonymous or interchangeable with the terms TRO, SRO, and IRO.

Summary of the 001 Clinical Study

Overview:

The "001 Study" was a prospective, longitudinal study conducted at seven sites in the United States. Adults aged 55 years or older with diagnosed NV-AMD in at least one eligible eye and best-corrected visual acuity of 20/320 or better were enrolled 1 week prior to a previously scheduled, routine clinic visit. Those who required anti-VEGF treatment for NV-AMD in the study eye at the screening visit, those who had any other retinal disease requiring steroidal or anti-VEGF treatment, or those with prior NVHO device use experience were excluded. One NV-AMD eye was determined to be the study eye.

The purpose of the study was the following: 1) to evaluate the agreement between in-office OCT macular scans versus the NVHO scans in the visualization of retinal fluid in the central 10 degrees of the macula, as determined by expert graders at a third-party reading center (RC); and 2) to evaluate the ability of participants to successfully self-image with the NVHO device. RC graders were masked to each other's determinations, to the source device, and to the participant ID number. Ordering of the scans was randomized. Disagreements between graders were adjudicated. IRF and SRF were graded as present when definite hypo-reflective space is observed in OCT B-scan images. IRF is anterior to the photoreceptor layer and SRF is posterior to the photoreceptor layer and anterior to the retinal pigment epithelium (RPE). The presence of confounding lesions (epiretinal membrane [ERM], macular hole, pseudocysts, outer retinal tubulations, hemorrhage, pigment epithelial detachments, subretinal hyper-reflective material [SHRM], geographic atrophy [GA], and hyper-reflective retinal spots or foci) was also assessed by the RC.

During the enrollment visit, participants underwent imaging with a clinic-based, spectral-domain OCT imaging system (CIRRUS HD-OCT) to establish a "baseline" status of the macula. After verification of eligibility during screening, participants were assigned an NVHO device. The assigned NVHO device was delivered to participants' homes. Participants set up the NVHO device using the onscreen tutorial. To continue in the study, participants must be able to achieve successful initial NVHO calibration. Continuing participants were instructed to self-image at home with the NVHO every day for five consecutive weeks, including on the days of scheduled office visits. Remote telephone technical support ("Notal Vision Diagnostic Clinic," NVDC) was available to participants. In-clinic visits were scheduled at Week 1 and Week 5. At these scheduled visits, CIRRUS HD-OCT imaging was performed and best-corrected visual acuity (BCVA), subjective symptoms, and adverse events were assessed. The daily NVHO scans of participants designated as without retinal fluid at baseline were reviewed by the reading center (RC). The RC triggered an alert for an interim clinic visit if fluid was identified on two consecutive NVHO scans from two consecutive days. CIRRUS HD-OCT images, BCVA, and any symptoms or adverse event information were also collected at these interim visits.

The primary effectiveness endpoints were positive and negative percent agreements (PPA, NPA) of central macular (central 3x3-mm area) fluid status between NVHO and RC-graded CIRRUS HD-OCT scans, success rate of initial NVHO setup, and success rate for NVHO self-imaging

attempts. The primary analysis of the PPA and NPA of visualizing Total Retinal Fluid (TRF) on NVHO volume scans was based on repeated measurements of the primary eyes using the optimal weighting method (Jung et al.) to test H_0: $p \leq 0.8$ vs. H_a: $p > 0.8$ with normal approximation and a two-sided significance level of 0.05. The secondary endpoints were the success rates of total (completed plus incomplete) and completed self-imaging transmission to the Notal Health Cloud. The safety outcomes of interest were any adverse events occurring during the conduct of the study.

Results:

198 participants were enrolled. Of these, seven (3.5%) were screen failures, eight withdrew consent prior to initiating participation (4.0%), two (1.0%) were exited due to inability to scan, and one (0.51%) was exited because of inability to return for follow-up. Therefore, 180 participants (90.9%) comprise the safety cohort. From the safety cohort, an additional 12 participants were excluded (10 due to device-use: inadequate image quality, self-calibration, and/or self-imaging problems; two who withdrew consent) to form the 168 participants (84.8%) in the "Visualization Analysis Population" (VAP) cohort (those who underwent clinic-based and NVHO imaging at Week-1, interim, or Week-5 visits). From the VAP cohort, another eight participants were excluded (seven due to not having NVHO scans with MSI score ≥2 and clinic-based OCT scans paired within 24 hours at Week-1, interim and Week-5 visits; one exited early due to difficulty with self-imaging) to form 160 participants (80.8%) in the "Modified Visualization Analysis Population" (mVAP) cohort. Primary analyses were based on the mVAP cohort.

Demographics, and relevant baseline clinical characteristics are shown in Tables 3 and 4. The majority of participants were White and not Hispanic or Latino.

Table 3: Demographics of Safety Population and mVAP – 001 Study

Demographics		**Safety Population N = 180**	**Modified Visualization Analysis Population N = 160**
Age	N	180	160
	Mean ± SD	77.1 ± 7.2	76.8 ± 7.2
	Median	77.5	77.0
	Min, Max	55, 92	55, 92
Gender	Male	78 (43.3%)	70 (43.8%)
	Female	102 (56.7%)	90 (56.3%)
Race	Asian	1 (0.6%)	1 (0.6%)
	Black or African American	4 (2.2%)	3 (1.9%)
	White	174 (96.7%)	155 (96.9%)
	Not Reported	1 (0.6%)	1 (0.6%)
Ethnicity	Not Hispanic or Latino	178 (98.9%)	158 (98.8%)
	Not Reported	2 (1.1%)	2 (1.3%)
Education	Less than High School Degree	8 (4.4%)	7 (4.4%)
	High School Degree	43 (23.9%)	38 (23.8%)

	Some college (no degree)	47 (26.1%)	44 (27.5%)
	College Degree (Associate or Bachelor's Degree)	51 (28.3%)	45 (28.1%)
	Graduate Degree	25 (13.9%)	21 (13.1%)
	Other[1]	6 (3.3%)	5 (3.1%)
Study Eye	OD	93 (51.7%)	82 (51.3%)
	OS	87 (48.3%)	78 (48.8%)

% = n / N × 100%.

[1] Including some graduate school, trade school, and tech school

Table 4: Baseline Characteristics of Safety Population and mVAP – 001 Study

Baseline Characteristics		Safety Population		Modified Visualization Analysis Population	
		Primary Eye[1] N = 180	Secondary Eye[1] N = 137	Primary Eye N = 160	Secondary Eye N = 123
AMD diagnostic[2]	AMD - Early AMD	0 (0.0%)	10 (7.3%)	0 (0.0%)	9 (7.3%)
	NV-AMD - non active (no fluid present)	92 (51.1%)	35 (25.5%)	84 (52.5%)	27 (22.0%)
	AMD - Intermediate AMD	0 (0.0%)	61 (44.5%)	0 (0.0%)	58 (47.2%)
	NV-AMD - active (fluid present)	88 (48.9%)	31 (22.6%)	76 (47.5%)	29 (23.6%)
Lens status	Phakia (cataract present)	65 (36.1%)	47 (34.3%)	61 (38.1%)	46 (37.4%)
	Pseudophakia	115 (63.9%)	90 (65.7%)	99 (61.9%)	77 (62.6%)
Ocular Media Assessment	Main vessels and the small vessels are clearly seen	179 (99.4%)	136 (99.3%)	159 (99.4%)	122 (99.2%)
	Both main and small vessels cannot be seen	1 (0.6%)	1 (0.7%)	1 (0.6%)	1 (0.8%)
Visual Distortions	Present	17 (9.4%)	7 (5.1%)	15 (9.4%)	7 (5.7%)
	Absent	163 (90.6%)	130 (94.9%)	145 (90.6%)	116 (94.3%)
Blurry Vision	Present	57 (31.7%)	28 (20.4%)	54 (33.8%)	26 (21.1%)
	Absent	123 (68.3%)	109 (79.6%)	106 (66.3%)	97 (78.9%)
Scotoma	Present	57 (31.7%)	28 (20.4%)	54 (33.8%)	26 (21.1%)
	Absent	123 (68.3%)	109 (79.6%)	106 (66.3%)	97 (78.9%)
Prior total # of Injections	N	180	137	160	123
	Mean ± SD	26.4 ± 26.5	12.1 ± 21.4	25.3 ± 26.6	12.0 ± 21.9
	Median	17.0	0.0	16.0	0.0
	Min, Max	0, 128	0, 125	0, 128	0, 125
Manifest Refraction Spherical Equivalent	N	151	113	137	104
	Mean ± SD	0.066 ± 1.924	0.044 ± 1.810	0.109 ± 1.881	0.135 ± 1.672
	Median	0.000	0.000	0.000	0.000
	Min, Max	-8.000, 5.000	-8.000, 5.000	-7.000, 5.000	-7.000, 5.000
Best Corrected	N	180	137	160	123

Visual Acuity	Mean logMAR (Snellen)	0.301 (20/40.0)	0.234 (20/34.3)	0.281 (20/38.2)	0.211 (20/32.5)
	SD logMAR	0.251	0.324	0.226	0.309
	Median logMAR (Snellen)	0.220 (20/33.2)	0.120 (20/26.4)	0.220 (20/33.2)	0.120 (20/26.4)
	Min logMAR (Snellen)	-0.10 (20/16.0)	-0.10 (20/16.0)	-0.10 (20/16.0)	-0.10 (20/16.0)
	Max logMAR (Snellen)	1.20 (20/320.0)	1.90 (CF)	1.04 (20/219.3)	1.90 (CF)
Best Corrected Visual Acuity category	20/40 or Better	110 (61.1%)	106 (77.4%)	102 (63.8%)	100 (81.3%)
	20/41 to 20/80	50 (27.8%)	20 (14.6%)	44 (27.5%)	16 (13.0%)
	20/81 to 20/200	14 (7.8%)	9 (6.6%)	12 (7.5%)	6 (4.9%)
	20/201 to 20/320	6 (3.3%)	1 (0.7%)	2 (1.3%)	1 (0.8%)
	Worse than 20/320	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)
Principal Investigator's retinal fluid assessment based on commercial OCT[2]	Both IRF and SRF	10 (5.6%)	3 (2.2%)	8 (5.0%)	3 (2.4%)
	SRF only	40 (22.2%)	13 (9.5%)	36 (22.5%)	13 (10.6%)
	IRF only	25 (13.9%)	14 (10.2%)	20 (12.5%)	11 (8.9%)
	No IRF nor SRF	105 (58.3%)	107 (78.1%)	96 (60.0%)	96 (78.0%)

% = n / N × 100%. Manifest refraction was not recorded at the initial phase of the study.

[1] Primary Eye = study eye. Secondary Eye = the AMD or NV-AMD fellow eye of the study eye

[2] AMD diagnostic findings were collected from participants' medical record. OCT fluid status is based upon review by PI of the OCT taken during the enrollment visit.

For the safety cohort (N=180), the success rate of initial NVHO setup with completion of the non-qualifying tutorial was 86.7% (95% CI 80.8% – 91.3%; 156/180). 24 participants (13.3%) who still performed NVHO self-imaging did not successfully complete tutorials for either the primary or secondary eyes. The success rate of NVHO self-imaging (i.e., completing the self-imaging regardless of completing imaging data transmission to Notal Health Cloud) was 96.1% (95% CI 92.2% – 98.4%). Seven participants (3.9%) did not self-image successfully. The rate of successful transmission of any self-imaging being transmitted to the Notal Health Cloud was 97.2% (95% CI, 93.6% – 99.1%) in study eyes and 94.9% (95% CI, 89.8% – 97.9%) in fellow eyes. The rate of successful transmission of completed self-imaging to the Notal Health Cloud was 96.7% (95% CI, 92.9% – 98.8%) in study eyes and 94.2% (95% CI, 88.8% – 97.4%) in fellow eyes. 31 of 180 participants (17.2%) encountered device errors and/or malfunctions that precluded self-imaging and necessitated a device exchange. 120 of 180 participants (66.7%) contacted the NVDC for technical support. The NVDC contacted 47 of 180 participants (26.1%) with low adherence to device use to remind them to perform self-imaging and 84 of 180 (46.7%) for technical support. The NVDC also contacted 173 of 180 participants (96.1%) to remind participants of an upcoming scheduled in-clinic study visit.

Of those in the safety cohort who did not discontinue after completion of the initial tutorial and device calibration and performed self-imaging (N=165), the mean MSI score of the first-completed, study-eye self-images ranged from 4.388 to 4.557 during the first week (study days 1 to 7), 4.47 to 4.57 during the second week (study days 8 to 14), 4.28 to 4.49 during the third week (study days 15 to 21), 4.32 to 4.45 during the fourth week (study days 22 to 28), and 3.64 to 4.35 during the fifth week (days 29 to 35). The proportion of participants who obtained a first-

completed NVHO study-eye scan with MSI <2 ranged from 0.6% to 4.3% during the first week (study days 1 to 7), zero to 3.7% during the second week (study days 8 to 14), zero to 6.4% during the third week (study days 15 to 21), 0.8% to 4.0% during the fourth week (study days 22 to 28), and 2.1% to 6.5% during the fifth week (days 29 to 35).

The following table (Table 5) shows the primary analysis of NVHO Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Retinal Hypo-reflective Spaces Visualization based on Retinal Hypo-reflective Spaces Visualized on the Cirrus 3mm×3mm Area Modified Visualization Analysis Population (including subjects with NVHO and Cirrus scans within 24 Hours apart).

The PPA was 0.864 (95% CI 0.802, 0.926; p=0.043) and NPA was 0.849 (95% CI 0.792, 0.907; p=0.094).

Table 5: Primary Analysis of NVHO PPA and NPA for Retinal Hypo-reflective Spaces Visualization

Total Retinal Hypo-reflective spaces (TRO)	**Positive Percent Agreement (PPA)**		**Negative Percent Agreement (NPA)**	
	Rate (95% CI)	**Two-sided p-value for H0: $P_P \leq 0.8$ vs. Ha: $P_P > 0.8$**	**Rate (95% CI)**	**Two-sided p-value for H0: $P_N \leq 0.8$ vs. Ha: $P_N > 0.8$**
# pairs of scans of # subjects	163 pairs of scans of 105 eyes with Cirrus = TRO		146 pairs of scans of 95 eyes with Cirrus = no TRO	
# NVHO scans with TRO	143		20	
# NVHO scans without TRO	19		124	
# NVHO scans not gradable	1		2	
Pragmatic estimation per repeated measurements using optimal weighting method, Pw[1,2]	0.864 (0.802, 0.926)	0.043	0.849 (0.792, 0.907)	0.094
Point estimates and 95% CIs per 2000 Cluster Bootstrap resampling* for PPA and NPA	0.877 [143/163] (95% CI, 0.819 – 0.929)		0.849 [124/146] (95% CI, 0.802 – 0.894)	

The NVHO and Cirrus scan pairs with a scan time difference of > 24 hours were excluded from the analysis.

* The mean and (2.5^{th}, 97.5^{th}) percentiles of 2000 Cluster Bootstrap samples with re-sampling of participants.

1 Article, Sin-Ho Jung, Seung-Ho Kang and Chul Ahn (2001), Sample size calculations for clustered binary data, Statist. Med. 2001; 20:1971–1982

2 Pragmatic estimation: PPA is based on all pairs of Cirrus and NVHO scans with Cirrus graded as with fluid (i.e., + or present) regardless of whether NVHO cannot be graded; NPA is based on all pairs of Cirrus and NVHO with Cirrus graded as without fluid (i.e., - or absent) regardless of whether NVHO cannot be graded. Colin B. Begg, Robert A. Greenest, and Boris Iglewicz (1986),

The Influence of Uninterpretability on the Assessment of Diagnostic Tests, J Chron Dis Vol. 39, No. 8, pp. 575-584.

51 interim visits for 51 of 180 participants (28.3%) were conducted in response to the daily RC review. An NV-AMD treatment was administered at 26 of the 51 interim visits (51.0%). (Note: The "001 Study" was not designed to demonstrate the ability of the NVHO device to serve as an "early detection tool.")

10 adverse events (AEs) were reported for six participants. Of these 10, four were considered serious (SAEs). All SAEs were non-ocular in nature (myocardial infarction, pulmonary edema, fall, COVID-19 infection). Two AEs in two participants were ocular in nature (ocular pain and redness at the site of an intravitreal injection; eyelid stye). No ocular AEs involving vision loss were reported. None of the AEs were considered related to the NVHO device, and all AEs resolved prior to study termination.
As noted above, the presence of confounding lesions was assessed by the RC.

Summary of the 006 Clinical Study

Overview:
The "006 Study" was a prospective, cross-sectional, observational, single-visit study conducted at six sites in the United States. Participants with diagnosed NV-AMD in at least one eligible eye and best-corrected visual acuity of 20/320 or better in the study eye were enrolled. There was no minimum or maximum age requirement for eligibility. Those who had any other retinal disease requiring steroidal or anti-VEGF treatment, CIRRUS HD-OCT scan on screening visit with a signal strength <6, or those with non-neovascular (i.e., "dry") AMD in the study eye were excluded. The presence of confounding lesions (epiretinal membrane [ERM], macular hole, pseudocysts, outer retinal tubulations, hemorrhage, pigment epithelial detachments, subretinal hyper-reflective material [SHRM], geographic atrophy [GA], and hyper-reflective retinal spots or foci) was not exclusionary. One NV-AMD eye was determined to be the study eye. The purpose of the study was the following: 1) to evaluate the agreement in estimated retinal fluid volume between manually segmented CIRRUS HD-OCT macular scans versus the Notal OCT Analyzer (NOA) algorithm analyzing NVHO scans; 2) to estimate the repeatability and reproducibility of the TRO parameter; 3) to evaluate the amount of overlap in segmentation of IRF and SRF between NOA and manual graders.

Demographic information and medical history were collected from enrolled participants. Manifest refraction, best-corrected Snellen visual acuity (BCVA) assessment, and assessment of media opacity were performed. Initial macular scanning with the CIRRUS HD-OCT was performed. One study eye per participant was selected. Participants then received a general overview on how to self-operate the NVHO device. Imaging without pharmacologic pupil dilation using CIRRUS HD-OCT and two NVHO devices was performed. The order of CIRRUS vs. NVHO imaging for each participant and the order of NVHO device use were randomized. Independent, masked graders from a third-party reading center (RC) performed manual segmentation of hypo-reflective spaces on the central 3×3-mm area of acceptable CIRRUS macular scans. Graders were masked to each others' determinations and to the participant ID

number. Ordering of the scans was randomized. SRF was defined as a hypo-reflective space located beneath the retina between the ISE (integrity of the inner segment ellipsoid band, or inner segment/outer segment [IS/OS] border) and RPE layers and IRF was defined as a hypo-reflective space located in the retina between the internal limiting membrane (ILM) and ISE layers.

The measurement variability of NOA-based volume estimates under repeatability conditions (i.e., within the same person using/operating the same NVHO device repeatedly) and reproducibility conditions (i.e., the same person using/operating different NVHO devices repeatedly) were determined using a random-effects analysis of variance (ANOVA) model. The agreement between NOA-based and CIRRUS-based volume estimates was calculated using Bland-Altman 95% limits of agreement (LOAs) and Deming regression analyses. The segmentation overlap analysis included calculation of the device-grader Dice coefficient for each grader averaged over cases and the calculation of the grader-grader Dice coefficient for each pair of graders averaged over cases. Since the Dice coefficient is undefined when both methods in the comparison do not provide a segmentation, those cases were excluded from the calculation of the average of Dice coefficients. To account for these excluded cases, the device-grader negative percent agreement (NPA) was calculated for each expert. Uncertainty of results was characterized by 95% confidence intervals representing case variability.

Results:

398 participants were enrolled. 11 (2.8%) were screen failures; therefore, the safety cohort (all eligible participants who underwent CIRRUS or NVHO scanning) is comprised of 387 participants. 78 (19.6%) exited from the study early (due mainly to inability to successfully calibrate the NVHO [N=57]). Participants who could not successfully complete either NVHO or CIRRUS imaging (or both) or whose scans did not have eligible fluid measurements were excluded from precision, agreement, and Dice coefficient analysis cohorts. The "Fluid Precision Analysis Population" and "Fluid Agreement Analysis Population" cohorts were comprised of 331 participants and the "Dice Analysis Population" was comprised of 336 participants.

Demographics, and relevant baseline clinical characteristics are shown in Tables 6 and 7. The majority of the participants were White and not Hispanic or Latino.

Table 6: Demographics of Safety Population and mVAP – 006 Study

Demographics		**Safety Population** **N = 387**	**Fluid Marking (DICE) Analysis Population** **N = 336**	**Fluid Agreement Analysis Population[1]** **N = 331**
Age	N	387	336	331
	Mean ± SD	76.2 ± 7.5	75.4 ± 7.4	75.5 ± 7.3
	Median	77.0	76.0	76.0
	Min, Max	53, 91	53, 91	53, 91
Gender	Male	158 (40.8%)	140 (41.7%)	137 (41.4%)
	Female	229 (59.2%)	196 (58.3%)	194 (58.6%)
Race	American Indian or Alaska Native	2 (0.5%)	1 (0.3%)	1 (0.3%)

	Asian	2 (0.5%)	1 (0.3%)	1 (0.3%)
	Black or African American	6 (1.6%)	5 (1.5%)	5 (1.5%)
	Native Hawaiian or Other Pacific Islander	1 (0.3%)	1 (0.3%)	1 (0.3%)
	White	370 (95.6%)	322 (95.8%)	317 (95.8%)
	Not Reported	6 (1.6%)	6 (1.8%)	6 (1.8%)
Ethnicity	Hispanic or Latino	9 (2.3%)	9 (2.7%)	9 (2.7%)
	Not Hispanic or Latino	375 (96.9%)	324 (96.4%)	319 (96.4%)
	Not Reported	3 (0.8%)	3 (0.9%)	3 (0.9%)
Education	Less than High School Degree	13 (3.4%)	11 (3.3%)	11 (3.3%)
	High School Degree	109 (28.2%)	87 (25.9%)	85 (25.7%)
	Some college (no degree)	80 (20.7%)	71 (21.1%)	70 (21.1%)
	College Degree (Associate or Bachelor's Degree)	125 (32.3%)	112 (33.3%)	111 (33.5%)
	Graduate Degree	52 (13.4%)	49 (14.6%)	48 (14.5%)
	Trade School	6 (1.6%)	5 (1.5%)	5 (1.5%)
	Other[2]	2 (0.5%)	1 (0.3%)	1 (0.3%)
Study Eye	OD	181 (46.8%)	160 (47.6%)	157 (47.4%)
	OS	206 (53.2%)	176 (52.4%)	174 (52.6%)

% = n / N × 100%.

[1] Fluid Agreement Analysis Population = Fluid Precision Analysis Population for this study

[2] Including some graduate school, trade school, and tech school

Table 7: Baseline Characteristics Safety, Fluid Marking and Fluid Agreement Analysis Populations

Baseline Characteristics		**Safety Population** N = 387	**Fluid Marking (DICE) Analysis Population** N = 336	**Fluid Agreement Analysis Population[1]** N = 331
AMD Diagnosis Based on Participants' Medical Record	AMD - Early AMD	1 (0.3%)	1 (0.3%)	1 (0.3%)
	AMD - Intermediate AMD	6 (1.6%)	4 (1.2%)	4 (1.2%)
	NV-AMD - active (fluid present)	372 (96.1%)	323 (96.1%)	319 (96.4%)
	NV-AMD - non active (no fluid present)	8 (2.1%)	8 (2.4%)	7 (2.1%)
Lens Status	Phakia (cataract absent)	6 (1.6%)	5 (1.5%)	5 (1.5%)
	Phakia (cataract present)	123 (31.8%)	119 (35.4%)	116 (35.0%)
	Pseudophakia	258 (66.7%)	212 (63.1%)	210 (63.4%)
Ocular Media Assessment	Main vessels and the small vessels are clearly seen.	357 (92.2%)	307 (91.4%)	305 (92.1%)
	Small vessels are invisible while main vessels can be seen.	30 (7.8%)	29 (8.6%)	26 (7.9%)
Prior Total # of Injections	N	359	313	310
	Mean ± SD	25.9 ± 25.6	25.7 ± 25.2	26.0 ± 25.2
	Median	17.0	18.0	18.0

	Min, Max	1, 142	1, 134	1, 134
	N (Unavailable)	28	23	21
Medication Most Recently Administered	Aflibercept (Eylea)	190 (49.1%)	167 (49.7%)	166 (50.2%)
	Bevacizumab (Avastin)	97 (25.1%)	85 (25.3%)	84 (25.4%)
	Brolucizumab (Beovu)	5 (1.3%)	4 (1.2%)	4 (1.2%)
	Other Investigational Drug	13 (3.4%)	12 (3.6%)	11 (3.3%)
	Ranibizumab (Lucentis)	47 (12.1%)	39 (11.6%)	39 (11.8%)
	Vabysmo (Faricimab-svoa)	7 (1.8%)	6 (1.8%)	6 (1.8%)
	Unavailable	28 (7.2%)	23 (6.8%)	21 (6.3%)
Spherical Equivalent	N	387	336	331
	Mean ± SD	-0.131 ± 1.686	-0.166 ± 1.745	-0.172 ± 1.749
	Median	0.000	0.000	0.000
	Min, Max	-7.500, 4.750	-7.500, 4.750	-7.500, 4.750
Best Corrected Visual Activity	N	387	336	331
	Mean logMAR (Snellen)	0.370 (20/46.9)	0.350 (20/44.8)	0.344 (20/44.2)
	SD logMAR	0.293	0.283	0.277
	Median logMAR (Snellen)	0.300 (20/39.9)	0.300 (20/39.9)	0.300 (20/39.9)
	Min logMAR (Snellen)	-0.10 (20/16.0)	-0.10 (20/16.0)	-0.10 (20/16.0)
	Max logMAR (Snellen)	1.20 (20/320.0)	1.20 (20/320.0)	1.20 (20/320.0)
Best Corrected Visual Activity	20/40 or Better	194 (50.1%)	178 (53.0%)	177 (53.5%)
	20/41 to 20/80	110 (28.4%)	92 (27.4%)	92 (27.8%)
	20/81 to 20/200	68 (17.6%)	55 (16.4%)	52 (15.7%)
	20/201 to 20/320	15 (3.9%)	11 (3.3%)	10 (3.0%)
Principal Investigator's Retinal Fluid Assessment Based on Commercial OCT	Both IRF and SRF	82 (21.2%)	73 (21.7%)	73 (22.1%)
	SRF only	123 (31.8%)	108 (32.1%)	109 (32.9%)
	IRF only	142 (36.7%)	121 (36.0%)	120 (36.3%)
	No IRF nor SRF	35 (9.0%)	29 (8.6%)	28 (8.5%)
	Unavailable	5 (1.3%)	5 (1.5%)	1 (0.3%)

% = n / N × 100%.

[1] Fluid Agreement Analysis Population = Fluid Precision Analysis Population for this study

The repeatability and reproducibility percent coefficient of variation (%CV) ranged from 24.6% to 436.4% and from 26.2% to 475.2%, respectively, for TRO <10 VU. For TRO >10 VU, repeatability %CVs ranged from 5.9% to 25.0%, and reproducibility %CVs ranged from 11.4% to 33.4%.

The following table (Table 8) show the device-grader Dice coefficient and NPA for each grader acting as the "reference standard".

Table 8: Descriptive Statistics of Eye-Level DICE Between NOA versus Graders and Graders versus Graders

Statistics	NOA vs. Grader 1	NOA vs. Grader 2	NOA vs. Grader 3	Grader 1 vs. Grader 2	Grader 1 vs. Grader 3	Grader 2 vs. Grader 3
Comparing NOA-Grader TRO DICE to Grader-Grader TRO DICE						
N*	278	289	299	279	297	298
Dice Mean ± SD	0.5819 ± 0.2958	0.5655 ± 0.3203	0.5196 ± 0.3182	0.6222 ± 0.2754	0.5453 ± 0.3018	0.6000 ± 0.2918
95% CI of DICE Mean	0.5470, 0.6168	0.5284, 0.6026	0.4834, 0.5558	0.5897, 0.6546	0.5108, 0.5797	0.5668, 0.6333
Dice Median	0.6802	0.6844	0.6123	0.7221	0.6274	0.6964
NPA	0.734 (58/79)	0.746 (47/63)	0.787 (37/47)	0.722 (57/79)	0.494 (39/79)	0.603 (38/63)
95% CI of NPA[1]	0.623, 0.827	0.621, 0.847	0.643, 0.893	0.609, 0.817	0.379, 0.609	0.472, 0.724
Comparing NOA-Grader SRO DICE to Grader-Grader SRO DICE						
N*	213	223	241	205	232	235
Dice Mean ± SD	0.5379 ± 0.3495	0.5394 ± 0.3550	0.4951 ± 0.3612	0.5670 ± 0.3283	0.4934 ± 0.3530	0.5558 ± 0.3403
95% CI of DICE Mean	0.4907, 0.5852	0.4925, 0.5862	0.4492, 0.5409	0.5218, 0.6122	0.4477, 0.5390	0.5120, 0.5995
Dice Median	0.6811	0.6799	0.6536	0.7161	0.6129	0.6956
NPA	0.764 (123/161)	0.801 (113/141)	0.856 (95/111)	0.814 (131/161)	0.646 (104/161)	0.716 (101/141)
95% CI of NPA[1]	0.691, 0.827	0.726, 0.864	0.776, 0.915	0.745, 0.871	0.567, 0.720	0.634, 0.789
Comparing NOA-Grader IRO DICE to Grader-Grader IRO DICE						
N*	160	172	224	180	231	229
Dice Mean ± SD	0.4594 ± 0.3139	0.4316 ± 0.3263	0.2972 ± 0.3107	0.5100 ± 0.3312	0.3631 ± 0.3358	0.4227 ± 0.3444
95% CI of DICE Mean	0.4104, 0.5084	0.3825, 0.4807	0.2563, 0.3381	0.4613, 0.5587	0.3196, 0.4067	0.3779, 0.4676
Dice Median	0.5429	0.5133	0.1970	0.6519	0.4059	0.5467
NPA	0.946 (176/186)	0.965 (164/170)	0.966 (112/116)	0.839 (156/186)	0.565 (105/186)	0.629 (107/170)
95% CI of NPA[1]	0.903, 0.974	0.925, 0.987	0.914, 0.991	0.778, 0.888	0.490, 0.637	0.552, 0.702

N* is the number of cases that have a segmentation from NOA or the Grader

[1] Exact CI per binomial distribution

The following table (Table 9) shows the device-grader and grader-grader PPA for each grader acting as the "reference standard."

Table Error! No text of specified style in document.9: Descriptive Statistics of Pixel-level Positive Percent Agreement of Study Eyes on NVHO Scan

"True"		Grader 1			Grader 2			Grader 3		
"Test"		NOA	Grader 2	Grader 3	NOA	Grader 1	Grader 3	NOA	Grader 1	Grader 2
TRO	N[1]	273	273	273	257	257	257	289	289	289
	Mean ± SD	0.5315 ± 0.2958	0.6147 ± 0.2676	0.7007 ± 0.2346	0.5919 ± 0.2686	0.7511 ± 0.2197	0.7262 ± 0.2140	0.4832 ± 0.3162	0.6278 ± 0.2989	0.5356 ± 0.3054
	95% CI of Mean	0.4963, 0.5668	0.5828, 0.6466	0.6727, 0.7286	0.5589, 0.6249	0.7241, 0.7781	0.6999, 0.7525	0.4466, 0.5198	0.5932, 0.6624	0.5002, 0.5709
	Median	0.6011	0.7049	0.7793	0.6600	0.8158	0.7926	0.5143	0.7207	0.6262
SRO	N[1]	195	195	195	175	175	175	225	225	225
	Mean ± SD	0.5584 ± 0.3147	0.5640 ± 0.3066	0.6727 ± 0.2478	0.6462 ± 0.2853	0.7580 ± 0.2502	0.7133 ± 0.2287	0.5011 ± 0.3615	0.6277 ± 0.3544	0.5019 ± 0.3567
	95% CI of Mean	0.5139, 0.6028	0.5207, 0.6073	0.6377, 0.7077	0.6036, 0.6887	0.7207, 0.7954	0.6792, 0.7474	0.4536, 0.5486	0.5811, 0.6742	0.4551, 0.5488
	Median	0.6667	0.6849	0.7639	0.7311	0.8478	0.7944	0.5875	0.7802	0.6400
IRO	N[1]	166	166	166	150	150	150	220	220	220
	Mean ± SD	0.3789 ± 0.2931	0.5606 ± 0.3186	0.7010 ± 0.2694	0.4209 ± 0.2812	0.6510 ± 0.2911	0.6799 ± 0.2694	0.2466 ± 0.2710	0.4187 ± 0.3408	0.3555 ± 0.3271
	95% CI of Mean	0.3340, 0.4239	0.5117, 0.6094	0.6597, 0.7422	0.3755, 0.4663	0.6040, 0.6979	0.6365, 0.7234	0.2106, 0.2826	0.3735, 0.4640	0.3120, 0.3989
	Median	0.4054	0.6793	0.8168	0.4616	0.7601	0.7533	0.1429	0.4770	0.3483

[1] Excluding eyes with 0 "True" segmentations

TRAINING

Upon first usage, the NVHO device runs a built-in tutorial. The tutorial consists of video clips which show the patient how to self-image followed by a practice phase in which the patient performs these tasks. The device subsequently performs a calibration for each eye to personalize the refractive error correction of the patient. Following the calibration, the patient is able to self-image.

LABELING

Device instructions for use were provided for patient and prescribing users of the device separately. The Notal Home OCT User Manual (patient user manual) included instructions for home use, including system unpacking and set up. It also included instructions for interacting with the device, including accessing an on-device tutorial and calibration procedure, regular image capture, and wireless transmission of images to the Notal Home OCT Web Viewer.

The Notal Home OCT Web Viewer User Manual (prescriber user manual) included information regarding the Notal OCT Analyzer (NOA) AI-based software application. This included a description of how to interact with the Web Viewer user interface, including Manufacturer Signal quality Index (MSI), notifications, device outputs, and information regarding accessing individual patient OCT data for review.

Several product warnings were included in labeling that carefully specify the intended patient population, that the device is intended for use by a single patient, that scans with poor image quality may be unreliable, and that the device cannot be used to replace or delay in-office assessment.

The labeling also included a summary of the clinical trial procedures, patient population, environment in which it was evaluated, and results.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a home monitoring ophthalmic imaging device.

Risks to Health	Mitigation Measures
Inaccurate results related to false negative findings, leading to missed clinician alerts and delayed disease management	Clinical performance testing Non-clinical performance testing Software description, verification, validation and hazard analysis Human factors validation testing Labeling
Inaccurate results related to false positive findings, leading to unnecessary medical procedures	Clinical performance testing Non-clinical performance testing Software description, verification, validation and hazard analysis Human factors validation testing Labeling
Operator failure to self-image and obtain images that meet input quality specifications, resulting in failure to monitor disease progression	Training Human factors validation testing Labeling
Ocular light toxicity	Non-clinical performance testing
Equipment malfunction leading to user injury (e.g., shock, burn, interference)	Electromagnetic compatibility (EMC) testing Electrical safety testing Labeling
Adverse tissue reaction	Biocompatibility evaluation

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the home monitoring ophthalmic imaging device is subject to the following special controls:

(1) Clinical performance testing must demonstrate that the device performs as intended for the stated indications for use under anticipated conditions of use. Testing must:
   (i) Evaluate accuracy of measurements and image annotations;

(ii) Evaluate the variability in output performance due to the end user and the device used; and
(iii) Evaluate the device at clinical sites that are independent of the sites used to train the software.

(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. Testing must include:
(i) Verification of image quality, field of view, and resolution; and
(ii) Optical radiation safety evaluation (including a description of the optical path and light sources).

(3) Performance testing must demonstrate the electromagnetic compatibility (EMC) and electrical, thermal, and mechanical safety of the device in the intended use environment.

(4) Software verification, validation and hazard analysis must be performed. Software documentation must include the following:
(i) A description of interactions between software and hardware;
(ii) A description of all inputs and outputs of the algorithm(s);
(iii) A description of software modules that score, label, detect, quantitate, characterize, or otherwise analyze and report results, both separately and as a total system;
(iv) A description of the data used to train and test software modules, including number of cases, sources (sites and data acquisition devices), demographics, and reference standard;
(v) A description of the expected impact of applicable image acquisition hardware characteristics on performance and associated minimum specifications; and
(vi) Mitigation measures to manage failure of any subsystem components with respect to incorrect patient reports and operator failures.

(5) Patient-contacting components of the device must be demonstrated to be biocompatible.

(6) A training program must be included with sufficient educational elements so that upon completion of the training program, the user can operate the device in the indicated environment of use.

(7) Human factors testing must demonstrate that the intended users can correctly use the device.

(8) Labeling must include:
(i) Instructions for home use, including instructions on how the home user obtains quality self-images, and an explanation of how the device performance is affected by user interaction;
(ii) Physician instructions for use, including a description of the outputs and all user-interface components;
(iii) Warnings regarding image acquisition factors that affect image quality;
(iv) A warning that the device should not be used to replace or delay in-office assessment; and
(v) A summary of the clinical performance testing conducted with the device, including a description of the patient population and environment in which it was evaluated.

BENEFIT-RISK DETERMINATION

The risks of the device are based on data collected in the clinical studies described above. They include false positives, false negatives, and failure to provide outputs. False positives may lead to unnecessary medical visits and/or procedures. False negatives and/or failure to provide outputs may lead to missed or delayed opportunities for disease monitoring and/or intervention.

The probable benefits of the device are also based on data collected in the clinical studies as described above. They include the ability to visualize the central macula in a home setting at a higher frequency than with currently available, in-clinic OCT imaging systems and the ability to identify, at home, hypo-reflective spaces that may be associated with worsening of neovascular age-related macular degeneration. It has not been demonstrated whether these benefits will result in improved visual outcomes.

Additional factors considered in determining probable risks and benefits for the Notal Vision Home Optical Coherence Tomography (OCT) System included: uncertainty, risk mitigation, and novelty of technology.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

> The Notal Vision Home Optical Coherence Tomography (OCT) System is an Artificial Intelligence (AI)-based Home Use device indicated for visualization of intraretinal and subretinal hypo-reflective spaces in a 10 by 10-degrees area centered on the point of fixation of eyes diagnosed with neovascular age-related macular degeneration (NV-AMD). In addition, it provides segmentation and an estimation of the volume of hypo-reflective spaces. The Notal Home OCT device is intended for imaging at home between regularly scheduled clinic assessments and not intended to be used to make treatment decisions or replace standard-of care regularly scheduled examinations and clinical testing as needed, including in-office imaging and assessments for changes in vision, by an ophthalmologist.

The probable benefits outweigh the probable risks for the Notal Vision Home Optical Coherence Tomography (OCT) System. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Notal Vision Home Optical Coherence Tomography (OCT) System is granted and the device is classified as follows:

Product Code: SAX
Device Type: Home monitoring ophthalmic imaging device
Regulation Number: 21 CFR 886.1600
Class: II