November 15, 2019

CooperVision, Inc.
Ms. Annette Nelson
Senior Regulatory Affairs Manager
5870 Stoneridge Drive
Pleasanton, CA 94588

Re: P180035
Trade/Device Name: MiSight 1 Day (omafilcon A) Soft (Hydrophilic) Contact Lenses for Daily Wear
Product Code: QIT
Filed: September 4, 2018
Amended: February 4, 2019; May 24, 2019; August 19, 2019; August 20, 2019

Dear Ms. Nelson:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the MiSight 1 Day (omafilcon A) Soft (Hydrophilic) Contact Lenses for Daily Wear. This device is indicated for the correction of myopic ametropia and for slowing the progression of myopia in children with non-diseased eyes, who at the initiation of treatment are 8-12 years of age and have a refraction of -0.75 D to -4.00 D (spherical equivalent) with ≤ 0.75 diopters of astigmatism. The lens is to be discarded after each removal. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

The sale and distribution of this device is restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 5 years. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of the PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. This report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the PMA device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Each report, identified as a PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. MiSight 1 Day Post-Approval Study for Effectiveness and Visual Symptoms (PAS001):
   You are required to provide post-approval effectiveness data to FDA on the *MiSight 1 Day* Contact Lens. You agreed to a study outline on November 1, 2019. *MiSight* 1 Day Effectiveness Post-Approval Study is designed to:

   - confirm in the U.S. population that there are clinically meaningful differences (super-superiority margin of 0.50D) in the mean change of cycloplegic refractive error and axial length change from baseline after three years of using *MiSight* 1 Day lenses among intended patient population compared to the mean changes in a control group using conventional daily disposable lenses;

   - estimate the effects of race, baseline cycloplegic spherical equivalent refractive error, and baseline age on the treatment effect;

   - assess the effects of the *MiSight* 1 Day on the patients' visual symptoms and the effects on patient activities of daily living, using an appropriately validated PRO measure; and adding specific endpoints and analyses to the study protocol to evaluate the rates of the more important symptoms; and

   - assess the stability of the myopia reduction over 1-year post-treatment among those who completed the 3-year confirmation study follow-up.

   The study population will consist of:
   children ages of 8-12, who have best corrected visual acuity of at least 20/25 bilaterally, with refractive error within the approved power range of *MiSight* 1 Day lenses (-0.75 D to – 4.00D spherical equivalent and ≤ 0.75 D of astigmatism at the initiation of treatment), who are free of ocular disease or abnormalities (including any corneal scar), and who are not under medication that would interfere with

contact lens wear, or are using or have used any pharmaceuticals or other methods for control of myopia will be identified for inclusion in the study. (Full statement in the protocol will exclude all patients who have any of the specific Contraindications in labeling.)
The study is intended to assess the effectiveness of the approval device in three phases.

Phase A: PRO
Develop new or modify existing PRO measures, and validate, using appropriate qualitative methods to ensure content coverage and understanding of the relevant concepts by patients and their parents.

Provide any necessary changes to the existing study protocol to incorporate this validation and modification of the PRO measure.

Phase B: US Study for Effectiveness and Visual Symptoms
A multicenter, double-blind, randomized prospective clinical trial will be conducted to confirm that there are clinically meaningful differences in the mean change of cycloplegic refractive error (super-superiority margin of 0.50D) and mean axial length change (super-superiority margin of 0.2 mm) from baseline after three years of using *MiSight* 1 Day lenses among intended patient population compared to the mean changes in a control group using conventional daily disposable lenses, adjusting for the effect of age, degree of initial myopia and the interaction effect between age and degree of initial myopia. Phase B will also assess the adverse visual effects of the *MiSight* 1 Day, as noted above.

This study will enroll a minimum of 675 patients in the *MiSight* 1 Day treatment group and 225 in the control group from all eligible patients in 25-35 US clinical sites and will have a minimum of 664 total number of evaluable patients (498 patients in the treatment group and 166 patients in the control group) completing 3 years of wear.

Phase C: Cessation Study
To assess the stability of the myopia reduction over 1-year post-treatment, all of those who completed the 3-year confirmation study follow-up will be continuously followed into a fourth year. A minimum number of 598 evaluable patients (with 448 in the treatment group and 150 in the control group) will complete this phase of the study (assuming a 10% attrition rate in the 4th year).

2. MiSight 1 Day Safety Post-Approval Study (PAS002):

You are required to provide post-approval safety data to FDA on the MiSight 1 Day Contact Lens. You agreed to a study outline on November 1, 2019. This study is designed to confirm that the incidence of Microbial Keratitis (MK) is lower than 0.002/patient-year among the intended patient population in the US.

This will be a cohort study nested within integrated health care and coverage organization systems or integrated (optometry/ophthalmology) eyecare practices. Consecutive subjects receiving the MiSight lens, who meet the inclusion criteria, will be prospectively identified to be included in the study, and will be consented for the use and release of their health care encounter data to be used for this safety study. Subsequent occurrence of the outcomes of interest will be identified using electronic health records and claims data within the integrated health care and coverage organization(s) or integrated

optometry/ophthalmology practices. Additionally, safety data from the *MiSight 1 Day Post-Approval Study for Effectiveness and Visual Symptoms* will be used to supplement this safety study.

The study population will consist of children ages 8-12, who are prescribed the MiSight lens for both eyes, who have best corrected visual acuity of at least 20/25 bilaterally, with refractive error within the approved power range of MiSight lenses (-0.75D to -4.00D spherical equivalent and ≤ 0.75D of astigmatism at the initiation of treatment), who are free of ocular disease or abnormities (including any corneal scar), and who are not under medication that would interfere with contact lens wear or any pharmaceuticals for control of myopia will be identified for inclusion in the study. (Children who have any of the specific contraindications in the labeling will not be included in the study.) Children that are being fitted for the MiSight and who will first start using the device at the time of study initiation or thereafter will be included in the analysis.

Data will be captured on the following endpoints: microbial keratitis, the incidence of loss of best-corrected visual acuity, the incidence of non-infectious infiltrative keratitis, and peripheral non-infectious ulcers. Safety data will be captured for all subjects through three years post first-fitting**.** A minimum follow-up of 8 months is required for each subject. All cases of MK among the enrollees will be identified and reported to the FDA.

Incidence rates per patient-year will be estimated with 95% confidence intervals for each endpoint listed above.

To estimate the microbial keratitis rate, accrual of 8,500 patient-years is needed. A minimum of 6,000 patient-years, from 2,000 prospectively identified subjects will be accumulated from the safety PAS, and a minimum of 2,500 patient-years will be accumulated from the subjects enrolled in the e*ffectiveness PAS.*

From the time of US product launch for the *MiSight 1 Day Lens,* you are required to meet the following timelines:

- First subject enrolled within 180 days
- 20% subject enrolled within 360 days
- 50% subject enrolled within 540 days
- 100% subject enrolled within 720 days
- Submission of Final study report: 3 months from study completion (i.e. last subject, last follow-up date)

From the time of US product launch for the *MiSight 1 Day Lens*, you are required to meet the following timelines:

- First subject consented within 180 days
- 20% subject consented within 360 days
- 50% subject consented within 540 days
- 100% subject consented within 900 days
- Submission of Final study report: 3 months from study completion (i.e. last subject, last follow-up date)

In addition, you are required to submit separate periodic reports on the progress of both post-approval studies, as follows:

- PAS Progress Reports every three (3) months until enrollment has started and every six (6) months until subject enrollment has been completed, and annually thereafter.

- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports (i.e., every 3 months), in addition to your periodic (6-months) PAS Progress Reports, until FDA notifies you otherwise.

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Be advised that failure to comply with any post-approval requirement, including the initiation, study design, endpoints, enrollment, completion, and reporting requirements outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.126(a).

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (https://www.fda.gov/media/71327/download).

Within 30 days of your receipt of this letter, you must submit PMA supplements that include complete protocols of your post-approval studies described above. Your PMA supplements should be clearly labeled as a PMA Post-Approval Study Protocol" as noted above and submitted to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement. You must also obtain approval of your PAS protocols within 60 days from the date of this order.

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to

UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Before making any change affecting the safety or effectiveness of the PMA device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" https://www.fda.gov/media/81431/download.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product postmarketing safety reporting is available at (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the postmarketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should

include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.
Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Scott E Steffen at 240-402-8795 or Scott.Steffen@fda.hhs.gov.

Sincerely,

Kesia Alexander

for Malvina B. Eydelman, M.D.
Director
OHT1: Office of Ophthalmic, Anesthesia,
Respiratory, ENT and Dental Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health