DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

January 8, 2014

Ocular Therapeutix, Inc.
Mr. Eric P. Ankerud, J.D.
Executive Vice President, Clinical,
Regulatory and Quality
36 Crosby Dr., Suite 101
Bedford, MA 01730

Re: P130004
ReSure® Sealant
Filed: February 19, 2013
Amended: February 19, June 11, June 28, July 30, August 27 and October 4, 2013
Procode: PFZ

Dear Mr. Ankerud:

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 ReSure® Sealant. This device is indicated for intraoperative management of clear corneal incisions (up to 3.5mm) with a demonstrated wound leak for which a temporary dry surface can be achieved, in order to prevent postoperative fluid egress from such incisions following cataract surgery with intraocular lens (IOL) placement in adults. 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.

The sale and distribution of this device are 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 this restriction on sale and distribution is 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 months. 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 this 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. Two copies of 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 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. Two (2) copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. In addition to the conditions outlined above, you must conduct two post-approval studies as described below:

1. Device Exposure Registry Study:

   The purpose of this study is to evaluate the incidence of endophthalmitis for cataract surgery patients treated with ReSure Sealant when used by a broad group of physicians. A prospective multicenter observational single-arm registry study will be conducted that will include up to 100 centers in the United States with enrollment of at least 4,857 patients treated with ReSure Sealant. The primary endpoint will be endophthalmitis. Patients will be identified as having undergone cataract surgery using the surgeon's standard techniques and if ReSure Sealant is applied the patient will be considered enrolled and their data will be linked to Medicare to ascertain if they are diagnosed or treated for endophthalmitis within 30 days of the procedure. Follow-up will consist of query of the Medicare database on at least an annual basis starting from the date Medicare data is available, for at least one year after enrollment of the last patient. A sample size of 4,857 achieves an alpha of 0.05 and approximately 82% power to detect a difference (P1-P0) of -0.0020 using a one-sided binomial test, where P0 is the proportion of endophthalmitis within 30 days under the null hypothesis (0.0040) and P1 is the proportion of endophthalmitis within 30 days under the alternative hypothesis (0.0020).

2. Clinical PAS:

   The purpose of this study is to evaluate the incidences of the major ocular adverse events (AEs) in the postmarket setting for cataract surgery patients treated with ReSure Sealant. A prospective multicenter observational single-arm study will be conducted in at least 598 patients enrolled at up to 40 centers. Patients enrolled in this study will be evaluated in the immediate post-operative period (Visit 1: Day 1 to Day 3) and again at approximately 4 weeks post-procedure (Visit 2: Day 20 to Day 40).

Perioperative observations to be recorded will include:

- Number of ReSure Sealant devices used,
- ReSure Sealant lot number(s),
- Concomitant suture use (before and/or after use of ReSure Sealant), and
- Ocular AEs (device related events recorded after the first application of ReSure Sealant).

The primary endpoint will be the following AEs occurring in the post-operative follow-up period:

- Anterior chamber cells greater than level 1+ persisting at Visit 2,
- Hypotony (</= 5 mmHg),
- Ocular discomfort (an Ocular Comfort Index (OCI) score greater than 51.7 or a within-person change from baseline of greater than 37.8), and
- Surgical reintervention.

The following ocular examinations will be performed:

- Intraocular Pressure (IOP), and
- Slit lamp examination with fluorescein staining including an assessment of ReSure Sealant presence.

Patients will complete an OCI questionnaire at the screening and follow-up visits. Positive responses to the OCI should be not be reported as endpoint events unless: (1) the OCI score is outside of normal limits for the post-cataract surgical period observed (i.e., an OCI score greater than 51.7 or a within-person change of 37.8 or more) and (2) ReSure Sealant is still present in the eye at the time that the event is reported. All endpoint ocular AEs, device-related ocular AEs, and Serious ocular AEs (including the nature, severity, seriousness, and relationship to ReSure Sealant) occurring during the course of the study will be documented.

A sample size of 598 achieves an alpha of 0.05 and 80% power to detect a difference (P1-P0) of -0.025 using a one-sided binomial test, where P0 is the proportion of individual primary endpoint adverse ocular events in the post-operative follow-up period under the null hypothesis (0.075) and P1 is the proportion of individual primary endpoint adverse ocular events under the alternative hypothesis (0.050).

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.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your post-approval studies. Your PMA supplements should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate 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. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm).

Please be advised that the results from these studies 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.

FDA would like to remind you that you are asked to submit separate PAS Progress Reports every six months during the first two years of the study and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

Before making any change affecting the safety or effectiveness of the 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" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

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, 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 www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, 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 www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

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 www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. 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 copies of all approved labeling in final printed form. Final printed 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 printed labeling is identical to the labeling approved in draft form. If the final printed 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 in 6 copies, 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
PMA Document Mail Center – WO66-G609
10903 New Hampshire Avenue
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If you have any questions concerning this approval order, please contact James Bertram, Ph.D. at (301) 796-6860.

Sincerely yours,

Christy L. Foreman -S

Christy Foreman
Office Director
Office of Device Evaluation
Center for Devices and Radiological Health