DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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

Mr. David S. Fernquist
Vice President, Regulatory Affairs
Glaukos Corporation
26051 Merit Circle, Suite 103
Laguna Hills, CA 9265

JUN 25 2012

Re: P080030
Glaukos iStent® Trabecular Micro-Bypass Stent (Models: GTS-100R, GTS-100L) and inserter (GTS-100i)
Filed: December 19, 2008
Amended: December 23, 2008, February 04, 2009, August 10, 2009, November 17, 2009, January 13, 2010, May 19, 2010, May 24, 2010, November 09, 2010, November 24, 2010, February 14, 2011, August 17, 2011
Procode: OGO

Dear Mr. Fernquist:

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 Glaukos iStent® Trabecular Micro-Bypass Stent (Models: GTS-100R, GTS-100L) and inserter (GTS-100i). This device is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication. 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 36 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" (please use this title even if the specified interval is more frequent than one year) 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 separate post-approval study (PAS) reports. As a condition of approval, you must conduct the following post-approval studies:

1. *Extended Follow-up of IDE Cohort Study*: The purpose of the study is to assess the long-term safety of the Glaukos® iStent® Trabecular Micro-Bypass Stent Models GTS100R and GTS100L in subjects enrolled in Glaukos IDE Study GC-003. Both the device group and control group will be followed for five years. Device subjects received the Glaukos iStent in conjunction with cataract surgery and controls subjects received cataract surgery alone. A remaining 255 patients from the original cohort of 290 patients enrolled for the GC-003 study are eligible to participate in this post-approval study.

   The main safety endpoint is the rate of sight-threatening adverse events at five years. Sight-threatening adverse events include: BCVA loss $\geq$ 3 lines, endophthalmitis, corneal decompensation, severe retinal detachment, severe choroidal hemorrhage, severe choroidal detachment and aqueous misdirection. The difference in the sight-threatening adverse event rates at 5 years between the treatment group and control group will be calculated and the corresponding one-sided 90% confidence limit will be provided based on normal distribution approximation.

   In addition, data on the following safety measures will be collected: postoperative ocular adverse events, IOP levels, medication use, best spectacle-corrected visual acuity (BSCVA), VF measurements and pachymetry, findings from slit-lamp, fundus and gonioscopic measurements, and loss of best spectacle corrected visual acuity of $\geq$ 1 line ($\geq$ 5 letters) at $\geq$ 3 months postoperative.

2. *New Enrollment Study*: This will be a prospective, randomized, concurrently controlled, parallel group, multicenter study to assess the long-term safety of the Glaukos® iStent® Trabecular Micro-Bypass Stent Model GTS100 R and GTS100L in conjunction with cataract surgery. The treatment group will receive implantation of one stent per study eye in conjunction with cataract surgery. The control group will receive cataract surgery only. The study will include subjects with mild to moderate open-angle glaucoma, who will be enrolled in 20 to 45 sites. A total of 360 subjects (one eye per subject) will be enrolled and

randomized with a 1:1 ratio, 180 will be randomly assigned to stent implantation in conjunction with cataract surgery and 180 will undergo cataract surgery only. Assuming a 20% loss of follow-up over 5 years, 288 subjects (or 144 per group) will be available for the main endpoint evaluation at 5 years.

The primary safety endpoint is the sight-threatening adverse events. The rate of sight-threatening adverse events over a five year postoperative period will be compared between the treatment and control group. In addition, data will be collected on: intraoperative and postoperative ocular adverse events, findings from IOP, BSCVA, VF, pachymetry, and specular microscopy measurements; findings from slit-lamp, fundus and gonioscopic measurements.

The effectiveness outcomes include IOP reduction $\geq$ 20% vs. baseline IOP without ocular hypotensive medication, and IOP $\leq$ 18 mmHg without ocular hypotensive medication at 24 months. The rate of these effectiveness outcomes will be compared between the treatment and control groups.

3. *Registry Study*: This will be a prospective, single-arm, multicenter registry of subjects implanted with GTS100 stents. A total of 500 consecutive subjects that receive implantation of GTS100 stents will be recruited at a maximum of 20 sites in the U.S. Subjects will be followed for three years from the date of implantation, to monitor the sight-threatening events that include BCVA loss $\geq$ 3 lines vs. screening, endophthalmitis, corneal decompensation, severe retinal detachment, severe choroidal hemorrhage, severe choroidal detachment, and aqueous misdirection. Other ocular adverse events such as increase in IOP of $\geq$ 10 mmHg vs. screening at any time postoperative or loss of best spectacle corrected visual acuity of $\geq$ 1 line ($\geq$ 5 letters) vs. screening at $\geq$ 3 months postoperative will also be assessed. Additional safety events of interest include findings from IOP, best spectacle corrected visual acuity, visual field, and pachymetry, and findings from optic nerve head imaging and gonioscopic examination

   The rate of sight-threatening adverse events at each visit will be calculated. The Kaplan-Meier (K-M) method will be used to estimate the sight-threatening adverse event rate at three year postoperative. The corresponding 95% confidence interval will also be provided. For other adverse events the Kaplan-Meier (K-M) method will also be used.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocol of your post-approval study. Your PMA supplement 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).

FDA would like to remind you that you are required 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).

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.

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.

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 triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm; clinical and statistical data: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm)

U.S. Food and Drug Administration
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10903 New Hampshire Avenue
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If you have any questions concerning this approval order, please contact LCDR Andrew Yang at (301) 796-3650.

Sincerely yours,

Kesia Alexander

for

Malvina B. Eydelman, M.D.
Director
Division of Ophthalmic, Neurological,
and Ear, Nose, Throat Devices
Office of Device Evaluation
Center for Devices and Radiological Health

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