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

Medinol Ltd.
c/o H. Semih Oktay, Ph.D.
President
CardioMed Device Consultants, LLC
5523 Research Park Drive, Suite 110
Baltimore, MD 21228

MAY - 1 2012

Re: P110004
Presillion *plus* CoCr Coronary Stent on RX System

Dear Dr. Oktay:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) completed its evaluation of your premarket approval application (PMA) and issued an approval order on April 12, 2012. We inadvertently made an error in the expiration dating for this device. Expiration dating for this device has been established and approved at 2 years, not 6 months.

We hope that this error has not inconvenienced you. If you have any questions about this corrective action, please contact Nicole Ibrahim, PhD at Nicole.Ibrahim@fda.hhs.gov or (301) 796-5171.

Sincerely yours,

/S/ Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health

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APR 12 2012

Medinol Ltd.
c/o H. Semih Oktay, Ph.D.
President
CardioMed Device Consultants, LLC
5523 Research Park Drive, Suite 110
Baltimore, MD 21228

Re: P110004
Presillion™ *plus* CoCr Coronary Stent on RX System
Filed: February 9, 2011
Amended: March 8, 2011, March 17, 2011, July 8, 2011, August 4, 2011, and December 19, 2011
Procode: MAF

Dear Dr. Oktay:

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 Presillion™ *plus* CoCr Coronary Stent on RX System. This device is indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease associated with stenotic lesions in de novo native coronary arteries (length ≤ 30 mm) with a reference vessel diameter of 2.50 mm to 4.00 mm.

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). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. 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 6 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 post-approval study reports (PAS). As a condition of approval, you have agreed to conduct two post-approval studies as described below:

1. *The Continued Follow-up of BLAST Placebo Cohort*: The study must be conducted as per agreement reached on January 24, 2012 (September 23, 2009, version 1.0, and updates on January 12, 2012). The prospective, observational, single arm study will consist of continued follow up of the premarket cohort of the placebo patients from the BLAST study who will be followed annually.

   The individual endpoints are major adverse cardiac events (MACE), clinically driven target lesion revascularization (TLR), target vessel failure (TVF), target lesion failure (TLF), all cause mortality, myocardial infarction (MI), composite cardiac death/MI, and stent thrombosis.

   The study population will consist of the patients in the BLAST placebo cohort treated with Presillion *plus* CoCr Coronary Stent on RX System per device labeling. Information on clinical outcomes will be collected annually through 5 years post-procedure on at least 80% of patients enrolled (excluding those discontinued due to death) in the BLAST clinical trial.

2. *The Enrollment of a New US Cohort Study:* The study must be conducted as per agreement reached on January 24, 2012 (P110004/A005, protocol version 0.4). The study will consist of a newly enrolled, non-randomized, multi-center, prospective, single arm clinical study of patients

treated with the Presillion *plus* CoCr Coronary Stent on RX System for the treatment of de novo stenotic lesions in native coronary arteries in the US population.

The primary effectiveness objective is to demonstrate that the 3-year incidence of TVF (cardiac death, target vessel myocardial infarction, or clinically driven target vessel revascularization) is less than the performance goal of 33% derived from development of a meta-analysis of five bare metal stent trials (standard of care). The expected rate for TVF at 3 years for the Presillion *plus* CoCr Coronary Stent on RX System is 22%.

A secondary objective is to assess long term safety. Secondary endpoints are all-cause mortality, cardiac death, all cause MI, target vessel MI, clinically driven TVR, acute success rates, and stent thrombosis.

The study population will consist of adult patients with symptomatic ischemic heart disease due to a single de novo stenotic lesion contained within native coronary artery with reference vessel diameter between 2.5 mm and 4.0 mm and lesion length $\leq$ 30 mm that is amenable to percutaneous revascularization with percutaneous coronary intervention with stent deployment. Clinical outcomes will be collected through 3 years post-procedure. In order to demonstrate that the Presillion *plus* CoCr Coronary Stent on RX System meets a TVF rate of 22% after three years, you must enroll at least 131 patients for 80% power (one sided α=0.05).

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.

FDA would like to remind you that for each of your PAS's, you are required to submit PAS Progress Reports every six months during the first two years and annually thereafter. Two copies, identified as a "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"
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm

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
Center for Devices and Radiological Health
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If you have any questions concerning this approval order, please contact Nicole Ibrahim, PhD at Nicole.Ibrahim@fda.hhs.gov or (301) 796-5171.

Sincerely yours,

for Bram D. Zuckerman, M.D.
Director
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Office of Device Evaluation
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