December 22, 2021

Conformal Medical, Inc.
Stephanie Whitnell
Director, Regulatory Affairs
15 Trafalgar Square, Ste. 101
Nashua, New Hampshire 03063

Re: G180189/S016/A001
Trade/Device Name: Conformal Left Atrial Appendage Closure (LAAC) System
Dated: December 1, 2021
Received: December 2, 2021
CMS Category: B
Annual Report Due: September 7, 2022

Dear Stephanie Whitnell:

The Food and Drug Administration (FDA) has reviewed the amendment to your Investigational Device Exemption (IDE) supplement proposing to conduct a new pivotal study for a significant risk device. You have corrected the deficiencies cited in our November 3, 2021 approval with conditions letter. FDA has determined you have provided sufficient data to support continuation of your human clinical study; this means that there are no subject protection concerns that preclude continuation of the investigation. Your supplement is therefore approved, and you may continue your investigation after you have obtained institutional review board (IRB) approval. Your investigation is limited to 100 US institutions and 250 US subjects.

Your IDE application has been approved as a staged study. You may request approval to expand enrollment in your study when you have submitted an IDE supplement which provides the following:

1. Section 10.3 of the submission provides an overview of outcomes to date with the CLAAS device implanted in the US and EU (Prague) early feasibility studies. While device performance overall appears encouraging in these studies, the aggregated safety data suggests a potentially higher-than-expected device-related thrombus rate. FDA believes that additional information is needed to better understand the device-related thrombus risk associated with your device and the proposed post-implant dual antiplatet therapy (DAPT) prior to exposing the full cohort of pivotal subjects to this risk. Additionally, significant delivery system design changes have been implemented since this data was collected, and information to assess the potential impact of these changes on clinical use and outcomes is warranted. To expand enrollment in your study, please provide the 45-day procedural and safety outcomes from the first 50 subjects to receive a CLAAS device (roll-in or randomized).

2. Section 10.5.3 of the submission and Attachment 8 summarize the accelerated durability testing conducted on the CLAAS device, in which 200M cycles of testing have been completed. To expand your study, please provide a complete report once 400M cycles are completed to establish the expected durability of the CLAAS device over a 10-year lifetime.

3. In your response to approval condition #7 of our November 3, 2021 letter, you clarify that the load force specification is defined as < 16 lbf, provide justification for this specification based on test failures previously observed due to high variability, and indicate that testing provided in report PR-056 was performed on final, finished CLAAS devices and that "all measures meet the minimum 95% confidence and 90% reliability". However, the testing in PR-056 did not measure load force against the defined specification, and a sample size of only N=15 per size was tested. Although testing provided in reports R-032 and R-034 in G180189/S012 included more samples and measurement of all simulated use forces (including load force), this testing was not performed on the final device configuration, including the final tether and tether routing configuration. Thus, FDA does not agree that you have established that your final device meets all simulated use specifications with 95% confidence and 90% reliability in accordance with your risk assessment (N=29 samples per size with no failures for pass/fail criterion). Therefore, please provide simulated use testing on the final, finished device demonstrating that all simulated use specifications are met with adequate confidence and reliability.

We would like to point out that approval of an IDE application does not ensure that the results of this investigation will provide a reasonable assurance of the safety and effectiveness of your device or assure a determination of clearance/approval for your premarket submission.

Your study may meet the definition of an applicable clinical trial, which requires mandatory registration and results information submission to http://www.clinicaltrials.gov. Please see the final rule "Clinical Trials Registration and Results Information Submission" (81 FR 64982; Sept. 21, 2016) and 42 CFR Part 11. For information on informed consent requirements related to applicable clinical trials set forth in 21 CFR 50.25(c), please see "Guidance for Sponsors, Investigators, and Institutional Review Boards Questions and Answers on Informed Consent Elements, 21 CFR 50.25(c)" at https://www.fda.gov/media/82634/download.

FDA will waive those requirements regarding prior approval of a supplemental IDE application for investigational sites (21 CFR 812.35(b)) provided that the total number of investigational sites does not exceed the limit identified in this letter. Under this waiver, the study may be initiated at new sites, up to the approved limit, and updated information required by 21 CFR 812.20(b) on participating investigators and associated Institutional Review Boards (IRBs) and the IRB approval documentation may be submitted all at once in your IDE annual progress report. You must, however, submit a supplemental IDE application, and receive FDA approval, prior to expanding the investigation beyond the site limit specified in this letter. In addition, you must maintain current records as required by 21 CFR 812.140 and submit reports as required by 21 CFR 812.150. If a reviewing IRB requires any significant changes in the investigational plan or in the informed consent that may increase the risks to subjects or affect the scientific soundness of the study, then this change must be submitted to FDA for review and approval prior to initiating the study at that investigational site (21 CFR 812.35). Minor changes requested by the IRB may be made without prior FDA approval. FDA also will waive the requirement for 6-month current investigator lists (21 CFR 812.150(b)(4)) provided that current investigator information is submitted every 12 months as part of the IDE annual progress report.

FDA acknowledges that your investigation will include foreign sites. FDA does not have jurisdiction over foreign sites; therefore, you may proceed at those foreign sites at your discretion. We encourage you however, to follow a uniform protocol at the domestic and the foreign investigational sites. Please note that FDA will accept data from studies conducted outside the United States if you demonstrate that the data are adequate to support a premarket submission (e.g., an IDE, or a marketing application or submission). Section 812.28 of the IDE regulation provides the requirements for studies conducted outside the United States that began on or after February 21, 2019, and are submitted in support of a premarket submission. For additional information please refer to the FDA Guidance "Acceptance of Clinical Data to Support Medical Device Applications and Submissions", available at: https://www.fda.gov/media/111346/download.

For studies conducted outside the United States that began before February 21, 2019, and are submitted in support of a premarket approval (PMA) application, FDA will accept the data if the data are valid and the investigators have conducted the studies in accordance with the "Declaration of Helsinki" or the laws and regulations of the country in which the study is conducted, whichever afford greater protection to the human subjects. If the country's standards are used, you must state in detail any differences between the country's standards and the "Declaration of Helsinki" and explain why the country's standards afford greater protection to the human subjects.

Furthermore, to export a device that is not in commercial distribution in the U.S. you must comply with Section 802 of the Federal Food, Drug and Cosmetic Act (the act). Detailed information regarding export requirements for investigational devices is available at: https://www.fda.gov/medical-devices/exporting-medical-devices/exporting-unapproved-devices.

For clarification regarding FDA decisions and recommendations for IDEs, please refer to the FDA guidance "FDA Decisions for Investigational Device Exemption Clinical Investigations: Guidance for Sponsors, Clinical Investigators, Institutional Review Boards, and Food and Drug Administration Staff," available at: https://www.fda.gov/media/81792/download.

In order for your study to serve as the primary clinical support for a future marketing approval or clearance, FDA has provided additional study design considerations as an attachment to this letter. These recommendations do not relate to the safety, rights or welfare of study subjects and they do not need to be addressed in order for you to conduct your study. You are reminded that prior to implementing any significant modifications to the approved investigational protocol you must obtain FDA approval, and, if appropriate, IRB approval for the changes.

We note that you have designed this protocol to collect safety and effectiveness data to support submission of a future PMA application. Regarding the statistics to be presented in the PMA, we expect analysis of the primary dataset to contain one line per unit (e.g., person, sample, observation) with clinical outcomes and baseline covariates. You should also provide the statistical program code which produces the above analyses and which clearly documents variable definitions and coding schemes, as well as the data, in an electronic format (e.g., SAS, S-Plus or R, Excel, ASCII).

If approved, it is likely that a post-approval study (PAS) may be requested as a Condition of Approval (CoA). As the original IDE cohort can sometimes be used to gather long-term safety and effectiveness data after market approval, we suggest you consider obtaining patient informed consent and IRB approval at the

initiation of the study so that enrolled subjects will be followed for a period of at least 5 years. FDA believes this may reduce patient loss to follow-up during the marketing application review process and keep many subjects available to participate in such a PAS if ordered. In addition, please note that other clinical studies apart from continued follow-up of IDE subjects, including prospective studies which enroll new patients, may also be required as CoA should a future marketing application be approved.

FDA encourages sponsors to collect clinical trial data in accordance with the Guidance for Industry: Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies (https://www.fda.gov/media/98686/download) and to enroll patients that would reflect the demographics of the affected population with regard to age, sex, race and ethnicity. Reference is made to 21 CFR 812.25(c) regarding description of patient population and to 21 CFR 814.15(b)(1) with regard to the need for data, including foreign data, to be applicable to the U.S. population and U.S. medical practice. We recommend that you include a background discussion of prevalence, diagnosis and treatment patterns for the type of disease for which your device is intended. This should include age-, sex-, race-, and ethnic-specific subgroup prevalence, identification of proportions of women and minorities included in past trials for the target indication, and a discussion of your plan to address any factors identified or suggested, which may explain potential for under-representation of women, minorities, and specific subgroups, if applicable. We recommend that you include a summary of this information in your protocol and investigator training materials. Consideration should be given to enrollment of investigational sites where recruitment of needed populations for study can be more easily facilitated.

Future correspondence concerning this application should be identified as an IDE supplement referencing the IDE number above, and must be submitted following eCopy guidelines to:

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

Information to help you understand the function and duties of a sponsor, titled, "Sponsor's Responsibilities for a Significant Risk Device Investigation," is available at: https://www.fda.gov/medical-devices/device-advice-investigational-device-exemption-ide/sponsors-responsibilities-significant-risk-device-investigations-nov-1995. Additionally, information which you should provide to participating investigators, titled, "Investigators' Responsibilities for a Significant Risk Device Investigation," is available at: https://www.fda.gov/medical-devices/device-advice-investigational-device-exemption-ide/investigators-responsibilities-significant-risk-device-investigations-nov-1995.

The Federal Food, Drug, and Cosmetic Act (the Act), as amended by section 1136 of the Food and Drug Administration Safety and Innovation Act (FDASIA), authorizes FDA to require an electronic copy (eCopy) for certain types of submissions. An eCopy is an exact duplicate of a paper submission, created and submitted on a CD, DVD, or other electronic media, accompanied by a single paper copy of your signed cover letter. This authorization applies to the original, amendments, supplements, and reports, as applicable, for your submission type.

For more information about FDA's eCopy program, including the technical standards for an eCopy, refer to the guidance document, "eCopy Program for Medical Device Submissions" at https://www.fda.gov/media/83522/download. In addition, we strongly encourage you to visit FDA's eSubmitter website at https://www.fda.gov/industry/fda-esubmitter/cdrh-esubmitter-program in order to develop an eCopy in accordance with the technical standards prior to sending it to FDA.

Background regarding the assigned CMS category and the process for requesting re-evaluation of the category is provided in guidance: "FDA Categorization of Investigational Device Exemption (IDE) Devices to Assist the Centers for Medicare and Medicaid Services (CMS) with Coverage Decisions," which is available at https://www.fda.gov/media/98578/download. Additional information about Medicare coverage related to Investigational Device Exemption (IDE) studies is available at https://www.cms.gov/Medicare/Coverage/IDE/index.html.

If you have any minor clarification questions concerning the contents of the letter, please contact Jennifer Bastijanic at 240-402-3049 or Jennifer.Bastijanic@fda.hhs.gov.

Sincerely,

Nicole G. Ibrahim -S

Nicole Ibrahim, Ph.D.
Director
DHT2B: Division of Circulatory Support,
Structural and Vascular Devices
OHT2: Office of Cardiovascular Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure
Additional Recommendations and Considerations

ADDITIONAL RECOMMENDATIONS AND CONSIDERATIONS

The recommendations and/or considerations below do not relate to the safety, rights or welfare of study subjects and they do not need to be addressed in order for you to conduct your study.

Study Design Considerations

FDA believes that additional modifications are needed in order for your study design to support marketing approval or clearance. We recommend, but do not require, that you modify your study to address the study design considerations listed in our November 3, 2021 letter.

If you intend to propose changes to your study to address these Study Design Considerations you should submit an IDE supplement.

Future Considerations

You should also give serious consideration to the future considerations listed in our November 3, 2021 letter, which FDA considers important for the support of a future submission.

The Future Considerations listed above are intended to assist in your plans for a future marketing application only. No response is necessary under this IDE, unless you wish to modify your device or study to address these concerns, in which case approval of an IDE supplement may be needed.

If you would like FDA's feedback on your plans for addressing any additional recommendations and considerations, please submit a Pre-Submission. Your submission should reference this IDE, identify the specific Study Design Considerations and/or Future Considerations you wish to discuss, and indicate your preferred feedback mechanism (i.e., email, meeting or teleconference). Additional information regarding Pre-Submissions is available in the Guidance for Industry and FDA Staff on Medical Devices: Requests for Feedback and Meetings for Medical Device Submissions at https://www.fda.gov/media/114034/download.