February 8, 2019

Intrinsic Therapeutics
℅ Glenn Stiegman
Senior Vice President, Clinical and Regulatory Affairs
Musculoskeletal Clinical Regulatory Advisers, LLC
1050 K Street NW, Suite 1000
Washington, District of Columbia 20001

Re: P160050
Trade/Device Name: Barricaid® Anular Closure Device (ACD)
Product Code: QES
Filed: November 14, 2016
Amended: December 6, 2016, August 16, 2017, August 13, 2018

Dear Mr. Stiegman:

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 Barricaid® Anular Closure Device (ACD). The Barricaid® ACD is indicated for reducing the incidence of reherniation, and reoperation in skeletally mature patients with radiculopathy (with or without back pain) attributed to a posterior or posterolateral herniation, and confirmed by history, physical examination and imaging studies which demonstrate neural compression using MRI to treat a large anular defect (between 4-6 mm tall and between 6-10 mm wide) following a primary discectomy procedure (excision of herniated intervertebral disc) at a single level between L4 and S1.

We are pleased to inform you that the PMA is approved. You may continue commercial distribution of the device upon receipt of this letter. 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 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 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.) Extended Follow-Up of the Barricaid® ACD Premarket Cohort for Lumbar Disc Herniation and Interaction with Other Risk Factors –

Based on the protocol summary agreed upon on February 8, 2019, the applicant will conduct an extended follow-up PAS, following the subjects from the pre-market study out to 10 years, to assess long term safety and effectiveness of the Barricaid® ACD, with a longer follow-up for a subset of subjects given certain additional risk factors. The PAS protocol is designed to examine the long-term survivorship of the Barricaid® ACD device when used in conjunction with limited discectomy. This study is also intended to monitor the natural history of endplate lesions due to interactions with the device, potential interactions with the development of osteoporosis, lesion growth and lesion stability. The study is also intended to investigate potential underlying mechanisms that may contribute to any additional growth through retrieval analysis and histological analysis of peri-prosthetic tissue. The prospective randomized multi-center OUS cohort used for the premarket application will follow all subjects annually out to 5 years with the existing clinical protocol.

All subjects will be followed at 7 and 10 years collecting the following information: patient questionnaires (VAS, ODI, SCORE), adverse event evaluation, symptomatic reherniation, femoral neck DEXA scan if required per SCORE osteoporosis screening questionnaire (subjects with SCORE of ≥ 6) and AP/lateral radiographs, lumbar MRI, low dose CT at index level to evaluate device subsidence, endplate lesions (size and growth measurements), device condition/migration, and reherniation at index level. The potential to require further extended follow-up will be determined at

the 10-year follow-up based on DEXA T Scores (femoral neck) and endplate lesion size as outlined in a Post-Approval Study Protocol.

The sponsor will analyze all Barricaid® ACD devices that are explanted as per the agreed upon retrieval analysis. Histopathologic analyses will be conducted on explanted tissue retrieved from secondary surgery at the index level as well as explanted Barricaid® ACD devices as a routine part of secondary surgery.

The hypotheses of this extended follow-up post approval study are that the Barricaid® ACD device remains safe and effective at 10 years, the Barricaid® ACD subjects do not have late or continued slow growth of lesions that lead to new or unexpected AEs or adverse clinical outcomes, and development of osteoporosis does not negatively impact the progression of lesions observed and does not lead to new or unexpected AEs or adverse clinical outcomes.

The FDA expects at least 85% follow-up at the 10-year timepoint to provide sufficient data to assess the long-term safety and effectiveness. A final report will be submitted within 6-months of the last subject visit.

2.) Histological and Retrieval Analysis of Material and Tissue From Retrieved (Explanted) Barricaid® ACD Devices in the Real World –

Based on the protocol summary agreed upon on February 8, 2019, the applicant will conduct a 5-year PAS on any explanted tissue or devices from real-world patients in the US, to investigate potential underlying mechanisms that may contribute to endplate lesion initiation and/or growth through retrieval analysis and histological analysis of retrieved implants and/or peri-prosthetic tissue. This study is also intended to evaluate causes of device failure (fracture, migration, dissociation and wear particulate).

All surgeons who are trained to use the Barricaid® ACD device will be instructed as part of their training to return partially or totally explanted devices (along with any surrounding tissue that is removed) to the sponsor for analysis. Retrieved devices and tissue samples will be collected from real world commercial use.

Clinical sites will be instructed to: collect tissue only if patient safety is not adversely affected; take physician narrative/ surgical notes regarding the condition of implant, relative location of tissue collected, etc.; take photographs of the device and any associated tissue; and immediately store device and tissue in formalin. All retrieved material and tissue will be visually inspected and photo documented. Device retrieval analysis will be conducted by an agreed upon protocol, while all tissue will be subject to histopathological examination by a qualified pathologist by an agreed upon protocol.

This evaluation is intended to generate data to further assess endplate lesion growth and/or other biological, radiographic or clinical observations. This will also evaluate device failure as it pertains to secondary surgical interventions and potential long-term survival.

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 http://www.fda.gov/devicepostapproval.

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" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm).

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes 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.

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final 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, http://www.fda.gov/udi.

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" http://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 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm and on combination product postmarketing safety reporting is available at (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm).

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 http://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 http://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 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 David Hwang at 301-796-3217 or David.Hwang@fda.hhs.gov.

Sincerely,

Randall G. Brockman -S

for William H. Maisel, MD, MPH
Director
Office of Device Evaluation
Center for Devices and Radiological Health

February 11, 2019

Intrinsic Therapeutics
℅ Glenn Stiegman
Senior Vice President, Clinical and Regulatory Affairs
Musculoskeletal Clinical Regulatory Advisers, LLC
1050 K Street NW, Suite 1000
Washington, District of Columbia 20001

Re: P160050
Trade/Device Name: Barricaid® Anular Closure Device (ACD)

Dear Mr. Stiegman:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) completed its review of your premarket approval application (PMA) and issued an Approval Order on February 8, 2019. We inadvertently made an error in the expiration dating approved for the device. The expiration dating for this device has been established and approved at 3 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).

We hope that this error has not inconvenienced you. If you have any questions about this corrective action, please contact David Hwang at 301-796-3217 or David.Hwang@fda.hhs.gov.

Sincerely,
for

Raquel A. Peat -S

Mark N. Melkerson
Director
Division of Orthopedic Devices
Office of Device Evaluation
Center for Devices and Radiological Health