June 29, 2023

ARUP Laboratories
Chelsea Welch
PharmaDx Quality and Regulatory Affairs Project Manager
500 Chipeta Way
Salt Lake City, Utah 84108-1221

Re: P190033
Trade/Device Name: AAV5 DetectCDx
Product Code: QWQ
Filed: December 23, 2019
Amended: January 7, 2020; February 11, 2020; March 5, 2020; April 3, 2020; May 8, 2020; May 18, 2020; October 29, 2021; September 30, 2022; November 14, 2022; May 30, 2023; June 29, 2023

Dear Chelsea Welch:

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 AAV5 DetectCDx. This device is indicated for:

> The AAV5 Total Antibody Assay for ROCTAVIAN (valoctocogene roxaparvovec-rvox) Eligibility in Hemophilia A ("AAV5 TAb Assay"), or AAV5 DetectCDx, is a qualitative in vitro diagnostic test by electrochemiluminescence intended for detection of antibodies in human plasma collected in 3.2% sodium citrate that bind to the adeno-associated virus serotype 5 (AAV5). The AAV5 TAb Assay is indicated as an aid in the selection of adult hemophilia A patients for whom ROCTAVIAN treatment is being considered. Patients that are anti-AAV5 antibody positive (result of Detected) are not eligible for treatment with ROCTAVIAN; patients that are anti-AAV5 antibody negative (result of Not Detected) are eligible for treatment with ROCTAVIAN. This assay is for professional use and is a single-site assay performed at ARUP Laboratories.

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. 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). 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.

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.

You have agreed to provide the following non-clinical information in a report, which may be followed by a PMA supplement where applicable.

1. ARUP Laboratories must provide data from a well-designed and well-controlled study to evaluate potential interference of assay results from high levels of cholesterol which can be found in patient samples. A minimum of three native samples with pre-existing anti-AAV5 antibodies defined as high negative, low positive, and high positive should be evaluated in the presence of 400 mg/dL cholesterol. If interference to the assay is observed in the presence of 400 mg/dL cholesterol, then a dose-response study must be performed to determine the highest concentration of cholesterol at which no interference to the assay is observed. The data from this study must be adequate to evaluate the potential interference caused by cholesterol in the intended use population. If interference is observed, you must provide information to support that the risk from the observed interference is adequately mitigated (e.g., revised labeling).

2. ARUP Laboratories must provide data from a well-designed and well-controlled study to evaluate potential interference of assay results from celecoxib/Celebrex, a COX-2 inhibitor and a commonly used medication in the hemophilia A patient population. A minimum of three native samples with pre-existing anti-AAV5 antibodies defined as high negative, low positive, and high positive should be evaluated in the presence of the highest celecoxib concentration in plasma during therapeutic treatment. If interference to the assay is observed in the presence of this highest drug concentration, then a dose-response study must be performed to determine the highest concentration of celecoxib at which no interference to the assay is observed. The data from this study must be adequate to evaluate the potential interference caused by celecoxib/Celebrex in the intended use population. If interference is observed, you must provide information to support that the risk from the observed interference is adequately mitigated (e.g., revised labeling).

3. ARUP Laboratories must implement a software change to mitigate the potential risk of a prozone/high-dose hook effect and provide documentation to demonstrate that this software change is validated for the safe and effective use of the AAV5 DetectCDx. Since a potential prozone/hook effect for the AAV5 DetectCDx was not evaluated in a non-clinical study for samples with Screen Index (SI) values > 90, if a patient sample with an SI value > 90 generates a Confirm Index (CI) value > 1.00 (typically indicative of a "Not Detected" result), the sample should still be considered "Detected." A software change will prevent reporting of a "Not Detected" result for patient samples with an SI value > 90.

The final study data, study conclusions, and labeling revisions should be submitted within four (4) months of the PMA approval date for items 1 and 2. Software documentation should be submitted within three (3) months of the PMA approval date for item 3.

Be advised that failure to comply with any post-approval requirement constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (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, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

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" https://www.fda.gov/media/81431/download.

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 post-marketing 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product post-marketing safety reporting is available at (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing 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 https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

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 Home Page located at https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. 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 Natasha Thorne at 240-402-0475 or Natasha.Thorne@fda.hhs.gov.

Sincerely,

Brittany W. Schuck -S

for

Timothy Stenzel, M.D., Ph.D.
Director
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health