December 19, 2023

AutoGenomics, Inc.
% Christine L. Brauer
Regulatory Affairs Consultant
Brauer Device Consultants, LLC
7 Trail House Court
Rockville, Maryland 20850

Re: P230032
Trade/Device Name: AvertD™ and AvertD™ Buccal Sample Collection Kit
Product Code: QZH
Filed: September 24, 2023

Dear Christine L. Brauer:

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 AvertD™. This device is indicated for:

> AvertD™ is a prescription, qualitative genotyping test used to detect and identify 15 genetic polymorphisms in genomic DNA isolated from buccal samples collected from individuals 18 years of age and older. The test may be used as part of a clinical evaluation and risk assessment to identify patients who may be at elevated risk for developing opioid use disorder (OUD). The test is indicated for use only in patients prior to receiving a first prescription of oral opioids for 4-30 days for acute pain, such as in patients scheduled to undergo a planned surgical procedure and who consent to having the test performed.
>
> The AvertD™ Buccal Sample Collection Kit is intended for use in the non-invasive collection, transport and storage of buccal specimens. DNA from the buccal sample will be suitable for use in AvertD. Buccal samples are collected by a qualified healthcare professional. For use only in individuals 18 years or older.

Based upon the information submitted, 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 available 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 all other applicable requirements, including those governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 12 months at 2-8°C for the AvertD BioFilmChip Microarray and AvertD Intellipac Reagent Module, 12 months at -15 to -30°C for the AvertD Amplification Mixture, and 1 year at ambient temperature for the AvertD Buccal Sample Collection Kit.

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 must 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, under 21 CFR 814.82(a)(9), 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 the following conditions of approval which are required as outlined in this order per 21 CFR 814.84(a):

1. AutoGenomics, Inc. (AGI) must mandate and facilitate robust training for health care providers prior to prescription of AvertD to patients. The purpose of this training is to ensure healthcare providers understand how to use the results from AvertD, understand the limitations associated with the test, and mitigate the risk of incorrect interpretation of test results. This training must include a description of the following:
    - AvertD (including sample collection and handling and the clinical workflow)
    - The AvertD indications for use (as well as patient populations it is not indicated for)
    - AvertD results, their interpretation, and how to use the results
    - The AvertD clinical study and results
    - Limitations with AvertD results

    As part of the training program, AGI must provide training on the informed consent process and obtain concurrence from healthcare providers that they will consent patients and provide the Fact Sheet for Patients and Other Recipients to the patient prior to collection of a sample for use with the genetic test.

2. AGI must provide a Fact Sheet (in addition to the AvertD package insert) to all health care providers prior to prescription of AvertD to patients. The Fact Sheet must inform healthcare

providers of the probable benefits and risks of use of AvertD. This fact sheet for healthcare providers must be provided at the time of training.

3. AGI must provide a Fact Sheet to be given to all patients prescribed AvertD. The Fact Sheet must advise patients of the probable benefits and risks of use of AvertD.

4. AGI must provide all healthcare providers a document with Frequently Asked Questions (and answers) that must be given to all patients prescribed AvertD. This document must include information on how the AvertD test works, how to interpret the results of AvertD, limitations with AvertD results, and what patient populations AvertD should not be used with.

In addition to the requirements outlined above, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

5. AGI must conduct a post-approval study of AvertD to assess the following:
    a. Device performance in the "real world" in the intended use population.
    b. Device performance across representative demographic subgroups (racial and ethnic).
    c. Impact of device results on provider prescribing practices (i.e., What do providers do when they have this result? How do prescribing habits change?)
    d. Patient and health care provider labeling comprehension to 1) ensure patients can understand on their own the meaning of the information they are given and 2) ensure providers understand indicated patient population, how to interpret test result and what to do with it.

    To address the post-approval study requirements cited above, AGI must complete a prospective study of patients tested by AvertD prior to receiving a first prescription of oral opioids for 4-30 days for acute pain, such as in patients scheduled to undergo a planned surgical procedure, and who consent to participate and have the test performed. The study must enroll a minimum of 3000 patients and be statistically powered to assess AvertD performance in demographically relevant subgroups in the United States population. Study participants must be followed for 5 years or until at least 50 OUD-positive patients are diagnosed per relevant demographic subgroup. Study participants must be clinically assessed at baseline and annually thereafter. Results of the AvertD must be compared to DSM-V based OUD diagnosis annually to assess device sensitivity and specificity in each subgroup and overall.

    i. AGI must develop and submit a complete post-approval study plan within 30 calendar days of the date of this order.
    ii. AGI must have an FDA approved post-approval study plan within 60 calendar days of this order.
    iii. AGI must provide interim reports to FDA every six months for the first two years of the post-approval study, and annually thereafter, from the date of the post-authorization study plan approval. By marketing your product, AGI agrees that the interim test performance data may be made public by FDA.
    iv. If any enrollment milestones are not met, AGI must submit a root cause analysis and a plan for completing the study on-time. In addition, AGI must begin submitting quarterly

enrollment status reports every 3 months in addition to AGI's periodic (6-month) interim reports, until FDA notifies AGI otherwise.

v. AGI must submit a final report to the agency within 3 months from study completion (i.e., last subject's last follow-up date).

You must obtain approval of your post-approval study (PAS) protocol(s) within 60 days from the date of this order. Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval study described below. Your PMA supplement should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted below 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.

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Be advised that failure to comply with any post-approval requirement, including related to training, health care provider and patient fact sheets, Frequetly Asked Questions document for patients, and the post-market approval study outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

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 in accordance with 21 CFR 814.46(a)(3)-(4).

Be advised that protocol information, interim and final results will be published on the Post-Approval Studies Program Database Webpage, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

In addition, the results from any post approval study should be included in the labeling as these data become available. Under 21 CFR 814.39, 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 Premarket Approval Application Order" (https://www.fda.gov/media/71327/download).

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 Part 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 available at 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. Additional information about changes that may require a PMA supplement are provided in 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.

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production and process controls (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 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 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 Part 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 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 Joseph Cleveland at Joseph.Cleveland@fda.hhs.gov.

Sincerely,

William H. Maisel -S

William H. Maisel, MD, MPH
Director, Office of Product Evaluation and Quality
CDRH Chief Medical Officer
Center for Devices and Radiological Health
Food and Drug Administration