Inova Genomics Laboratory 4/4/19

U.S. FOOD & DRUG ADMINISTRATION

10903 New Hampshire Avenue
Silver Spring, MD 20993

WARNING LETTER

VIA UNITED PARCEL SERVICE

Ramaswamy Iyer, Ph.D.
Director
Inova Genomics Laboratory
3300 Gallows Road
Claude Moore Building, 2nd Floor
Falls Church, VA 22042

April 4, 2019

Dear Dr. Iyer:

The Food and Drug Administration (FDA) has learned that your firm is marketing the MediMap ADHD, the MediMap Mind, the MediMap Plus, the MediMap Heart, and the MediMap Baby (collectively the MediMap tests) in the United States without marketing clearances or approvals, in violation of the Federal Food, Drug, and Cosmetic Act (the Act).

Under section 201(h) of the Act, 21 U.S.C. § 321(h), the MediMap tests are devices

because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body.

Your firm markets on its website (https://www.inova.org/medimap/tests) the MediMap tests as genetic tests for predicting medication response, reducing negative side effects from certain medications, discovering the right drug and right dose for a patient, and avoiding trial-and-error prescribing by healthcare providers by testing patient receptivity to drugs that treat specific conditions. For example, your firm markets the MediMap Plus (https://www.inova.org/medimap/plus) as providing insights into how a patient will respond to a variety of drugs including those used for anesthesia, cancers, infections, attention- deficit/hyperactivity disorder, depression, anxiety, and diabetes. The MediMap Baby is marketed for testing newborns to analyze genes that influence response to 24 medications and provide guidance in prescribing safer and more effective medications (https://www.inova.org/medimap/baby). In addition, your website (https://www.inova.org/medimap/FAQ) indicates that test reports generated by your MediMap tests provide "actionable and informational guidance" and that "Healthcare providers can use these results confidently in making treatment decisions."

FDA is concerned that the clinical validity**[1]** of your MediMap tests has not been established for their intended uses. Specifically, we are unaware of data establishing the relationships between the genotypes assessed by your tests and your assertions regarding drug response for multiple drugs. For example, the relationship between CYP2C19 genotype and drug response to escitalopram and sertraline is not established and this relationship is not described in the FDA- approved labeling for these drugs.

Given these issues, these tests pose significant public health concerns as inaccurate test results could impact the decision-making of healthcare providers and patients in ways that are seriously detrimental to patient health.**[2]** Healthcare providers may make inappropriate treatment decisions based on these test results, including inappropriate dosing adjustments, prescribing an ineffective therapy, and not prescribing a therapy that could benefit the patient. Such inappropriate treatments could lead to immediate serious health consequences for the patient. In the case of escitalopram and sertraline, for example, such inappropriate treatments pose a significant risk of illness, injury, or death where healthcare providers may avoid prescribing or may prescribe insufficient doses of these potentially life-saving antidepressant drugs to severely depressed, and/or suicidal patients.

Further, according to your website (https://www.inova.org/medimap/physicianinfo), the MediMap tests may be ordered by a lab physician in which case test results are provided directly to patients. This could lead to patients inappropriately increasing, decreasing, or stopping their medication without their physician's involvement, which

poses significant risks to patient safety. For example, abrupt cessation of antidepressants (e.g., escitalopram, sertraline) could lead to (1) illness, injury, or death due to withdrawal symptoms, (2) relapse of depression, and (3) reduced effectiveness of the drug if the drug needs to be re-started with the patient. Your MediMap Plus test also presents a significant risk of hypoglycemia, a potentially immediate life-threatening event, if results lead patients to inappropriately increase their dosage of glucose lowering drugs (e.g., nateglinide, glipizide). The MediMap Plus test also provides results for multiple opioid medications (e.g., codeine, dihydrocodeine, fentanyl, hydrocodone, methadone, morphine, oxycodone, tramadol, carisoprodol, and tizanidine) that are used to treat pain. If a patient uses inaccurate test results to inappropriately increase the dose of these medications, the patient has an increased risk of immediate respiratory depression and death.

FDA notified your firm of the Agency's concerns regarding your tests during our March 13, 2019 teleconference, and requested that your firm respond in writing by March 25, 2019. Specifically, FDA requested that your firm change the MediMap tests and labeling to address the concerns outlined in FDA's November 2018 safety communication, including removing from the labeling (e.g., patient test reports and promotional material) claims regarding drug responses for specific medications unless and until FDA reviews the information submitted to support such claims and grants marketing authorization. In your March 21, 2019 written response, you declined to commit to such changes. Your response states that the MediMap tests are laboratory developed tests (LDTs) and that "Inova believes it is properly operating within the scope of FDA's LDT exemption and thus is not subject to FDA's premarket review or labeling requirements."

FDA has not created a legal "carve-out" for LDTs such that they are not required to comply with the requirements under the Act that otherwise would apply. FDA has never established such an exemption. As a matter of practice, FDA, however, has exercised enforcement discretion for LDTs, which means that FDA has generally not enforced the premarket review and other FDA legal requirements that do apply to LDTs. Although FDA has generally exercised enforcement discretion for LDTs, the Agency always retains discretion to take action when appropriate, such as when it is appropriate to address significant public health concerns.

Based on the above, FDA has determined that the MediMap tests are adulterated under section 501(f)(1)(B) of the Act, 21 U.S.C. § 351(f)(1)(B), because your firm does not have an approved application for premarket approval (PMA) in effect pursuant to section 515(a) of the Act, 21U.S.C. § 360e(a), or an approved application for an investigational device exemption under section 520(g) of the Act, 21 U.S.C. § 360j(g). The MediMap tests are also misbranded under section 502(o) of the Act, 21 U.S.C. § 352(o), because your firm did not notify the Agency of its intent to introduce the devices into commercial distribution, as required by section 510(k) of the Act, 21 U.S.C. § 360(k). For a device requiring premarket approval, the notification required

by section 510(k) is deemed satisfied when a PMA is pending before the Agency. (See 21 CFR 807.81(b)). Information that may be helpful in preparing a premarket submission is available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/defaul The FDA will evaluate the information that your firm submits and decide whether the test may be legally marketed.

Your firm should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and civil money penalties.

Please notify this office in writing within fifteen (15) business days from the date you receive this letter of the specific steps your firm has taken to correct the noted violations, as well as an explanation of how your firm plans to prevent these violations, or similar violations, from occurring again.

Your response should include documentation of the corrections and/or corrective actions (including those that address systemic problems) that your firm has taken. If your firm's planned corrections and/or corrective actions will occur over time, please include a timetable for implementation of those activities. If corrections and/or corrective actions cannot be completed within fifteen business days, state the reason for the delay and the time within which these activities will be completed. Your firm's response should be comprehensive and address all violations included in this Warning Letter. If you continue to believe that your tests are not in violation of the Act, include your reasoning and any supporting information for our consideration.

Your firm's response should be sent to:

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

Refer to the reference number CMS577422 when replying. We remind you that only written communication is considered as official. If you have any questions about the contents of this letter, please contact: Brittany Schuck, Ph.D. at Brittany.Schuck@fda.hhs.gov or 301-796-5199.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your firm's facility. It is your firm's responsibility to ensure compliance with applicable laws and regulations administered by FDA.

Sincerely yours,
/S/
Timothy Stenzel, M.D., Ph. D.
Director
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

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[1] This letter focuses on issues relating to the clinical validity of the tests and not the analytical validity of the MediMap tests.

[2] We note that the concerns regarding specific drugs or drug classes included in this letter are not intended to be an exhaustive discussion of FDA's concerns with the MediMap tests.

More in Warning Letters

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
1-888-INFO-FDA (1-888-463-6332)