



January 23, 2019

23andMe, Inc.  
Adam Odeh  
Regulatory Affairs Manager  
899 W. Evelyn Ave.,  
Mountain View, California 94041

Re: DEN180028

Trade/Device Name: 23andMe Personal Genome Service (PGS) Pharmacogenetic Reports  
Regulation Number: 21 CFR 862.3364  
Regulation Name: Pharmacogenetic assessment system  
Regulatory Class: Class II  
Product Code: QDJ  
Dated: June 4, 2018  
Received: June 5, 2018

Dear Adam Odeh:

This letter corrects our letter dated October 31, 2018.

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the 23andMe Personal Genome Service (PGS) Pharmacogenetic Reports, an over-the-counter device with the following indications for use:

The 23andMe Personal Genome Service (PGS) is a qualitative genotyping assessment system applied to genomic DNA isolated from human saliva collected using the Oragene Dx OGD-500.001 to simultaneously detect, report, and interpret genetic variants in a broad multigene test. The assessment system is intended to enable users to access information about their genetics that could aid discussions with a healthcare professional. The 23andMe Personal Genome Service Pharmacogenetic Reports are indicated for reporting of the following variants:

Gene	Variant(s)
CYP2C19	*2, *3, *17
CYP2C9	*2, *3, *5, *6, rs7089580
CYP3A5	*3
UGT1A1	*6, *28
DPYD	*2A, rs67376798
TPMT	*2, *3C
SLCO1B1	*5

CYP2D6 \*2, \*3, \*4, \*5, \*6, \*7, \*8, \*9, \*10, \*11, \*15, \*17, \*20, \*29, \*35, \*40, \*41

This report is for over-the-counter use by adults over the age of 18 and provides genetic information to inform discussions with a healthcare professional about metabolism of therapeutics. This report describes if a person has variants associated with metabolism of some therapeutics, but does not describe if a person will or will not respond to a particular therapeutic, and does not describe the association between detected variants and any specific therapeutic. The PGS Pharmacogenetic Reports are not a substitute for visits to a healthcare professional. The information provided by this report should not be used to start, stop, or change any course of treatment.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact [CDRHProductJurisdiction@fda.hhs.gov](mailto:CDRHProductJurisdiction@fda.hhs.gov). FDA concludes that this device should be classified into Class II. This order, therefore, classifies the 23andMe Personal Genome Service (PGS), and substantially equivalent devices of this generic type, into Class II under the generic name Pharmacogenetic assessment system.

FDA identifies this generic type of device as:

**Pharmacogenetic assessment system.** A pharmacogenetic assessment system is a qualitative in vitro molecular diagnostic system intended to detect nucleic acid variants isolated from human specimens for the purpose of assessing the presence of genetic variants that impact the metabolism, exposure, response, risk of adverse events, dosing, or mechanisms of prescription or over-the-counter medications. The intended use of the device must not include an indication for use in supporting or sustaining human life, being of substantial importance in preventing impairment of human health, or presenting a potential, unreasonable risk of illness or injury.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On June 5, 2018, FDA received your De Novo requesting classification of the 23andMe Personal Genome Service (PGS). The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the 23andMe Personal Genome Service (PGS) into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the

device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the 23andMe Personal Genome Service (PGS) can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Identified Risks to Health	Identified Mitigations
Incorrect test results (false positive or false negative results)	Special controls (1), (2), (3), (4), and (5)
Incorrect interpretation of test results	Special controls (1)(ii), (2), (3), (4), (5) and (6)
Incorrect action based on test results	Special controls (1)(ii), (2), (3), (4), and (6)

In combination with the general controls of the FD&C Act, the pharmacogenetic assessment system is subject to the following special controls:

(1) Design verification and validation must include:

- (i) Data appropriate, as determined by FDA, to demonstrate the analytical accuracy and reliability of the device in intended use specimens, including but not limited to precision, reproducibility, accuracy, limits of detection, and interferences. This information must include:
  - (A) Data demonstrating appropriate, as determined by FDA, reproducibility for each genotype using each claimed sample type. Reproducibility data shall be evaluated using specimens collected and processed in a manner consistent with the device's instructions for use, or, as determined by FDA, an appropriate alternative sample panel.
  - (B) Analytical data demonstrating the limits of detection, including the minimum amount of input DNA that will consistently produce accurate results.
  - (C) Data demonstrating no clinically significant effects from endogenous and exogenous interferences relevant to each intended use specimen type. Interference data must also include an assessment of potentially interfering genetic sequences (e.g., variants proximal to the variant of interest, pseudogenes).
  - (D) Validation data appropriate, as determined by FDA, to support specimen collection and handling claims.
  - (E) Clinical data generated in intended use patient populations demonstrating the pharmacogenetic association between the genetic variant tested and any clinical claims or therapy-related recommendations associated with that genotype.
- (ii) Results from an appropriate, as determined by FDA, user comprehension study that demonstrate the intended user can use the device safely. The user comprehension study must be designed to include the following:

- (A) Study participants from a statistically sufficient sample size and a demographically diverse (e.g., age, education level) population that is representative of the intended use population and naïve to use of the device, and
- (B) An evaluation of all result comprehension concepts that are critical for safe use of the device.

(2) The 21 CFR 809.10 labeling must include:

- (i) Clear information, written in language appropriate for the intended user, that describes instructions for how test results should be interpreted. These instructions must be supported by valid scientific evidence and include:
  - (A) Appropriate explanation of the claimed pharmacogenetic associations for all variants included in the test, any relevant variants not included in the test (e.g., that may contribute to false negative results), and specific considerations by ethnicity, and
  - (B) Appropriate explanation of non-genetic and non-tested genetic factors that may impact interpretation of the test results;
- (ii) Detailed descriptions of analytical performance including, as applicable, precision, reproducibility, accuracy, limits of detection, and interferences as specified in paragraph (b)(1)(i) of this section, in language appropriate for the intended user;
- (iii) A warning statement that the patient should not use the test results to stop or change any medication, and that medications should always be taken as prescribed by a healthcare professional;
- (iv) A limiting statement explaining that this test is not intended to inform the patient about their current state of health, including whether or not the patient should or should not take a medication, or how much of a medication the patient should take, as appropriate;
- (v) A warning statement that the test does not diagnose any health conditions and is not a substitute for visits to a doctor or other healthcare professional; and
- (vi) A prominent and conspicuous limiting statement that the test provides only a preliminary test result that needs to be confirmed using an independent pharmacogenetic test without such a limitation prior to making any medical decisions. Alternatively, appropriate design verification and validation activities, including the generation of robust analytical data demonstrating appropriate analytical accuracy and reliability of test results for each genetic variant included in the test report, must be performed that demonstrate that the test can be used to make well-informed clinical decisions.

(3) The test report must include an appropriate description of how the test results should be used by healthcare providers who may receive the test results from their patients, as applicable.

(4) Publicly available pre-purchase labeling with unrestricted access that contains the following information must be provided:

- (i) A clear description of the test and its technology, the genotypes detected, and relevant clinical claims associated with each genotype;
  - (ii) A clear description of what information the test will provide. This includes, but is not limited to, variant information, the limitations associated with the test, and any precautionary information about the test the user should be aware of before purchase; and
  - (iii) A discussion of answers to frequently asked questions that is sufficient to provide intended users with an appropriate understanding of information specific to each pharmacogenetic association that is claimed.
- (5) The genetic test must use a sample collection device that is FDA-cleared, -approved, or classified as 510(k) exempt, with an indication for *in vitro* diagnostic use in DNA testing.
- (6) The intended use of the device must not include an indication for use in supporting or sustaining human life, being of substantial importance in preventing impairment of human health, or presenting a potential, unreasonable risk of illness or injury.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the pharmacogenetic assessment system they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD & C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD & C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/>) and CDRH Learn (<http://www.fda.gov/Training/CDRHLearn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<http://www.fda.gov/DICE>) for more information or contact DICE by email ([DICE@fda.hhs.gov](mailto:DICE@fda.hhs.gov)) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Brittany Schuck at 301-796-5199.

Sincerely,

Courtney H. Lias, Ph.D.  
Director  
Division of Chemistry and Toxicology Devices  
Office of In Vitro Diagnostics  
and Radiological Health  
Center for Devices and Radiological Health