January 18, 2019

23andMe, Inc.
Sarah Rys
Senior Manager, Regulatory Affairs
899 W. Evelyn Ave., CA
Mountain View, California 94041

Re: K182784
Trade/Device Name: MUTYH-Associated Polyposis (MAP)
Regulation Number: 21 CFR 866.6090
Regulation Name: Cancer Predisposition Risk Assessment System
Regulatory Class: Class II
Product Code: QAZ
Dated: September 28, 2018
Received: October 1, 2018

Dear Sarah Rys:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 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 Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, 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) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Reena Philip -S

Reena Philip, Ph.D.
Director
Division of Molecular Genetics and Pathology
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K182784

Device Name
23andMe Personal Genome Service (PGS) Genetic Health Risk Report for MUTYH-Associated Polyposis (MAP)

Indications for Use *(Describe)*
The 23andMe Personal Genome Service (PGS) uses qualitative genotyping to detect select clinically relevant variants in genomic DNA isolated from human saliva collected from individuals ≥18 years with the Oragene Dx model OGD500.001 for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for MUTYH-Associated Polyposis. The 23andMe PGS Genetic Health Risk Report for MUTYH-Associated Polyposis is indicated for reporting of the Y179C and the G396D variants in the MUTYH gene. The report describes if a person is at increased risk of developing colorectal cancer. The two variants included in this report are most common and best studied in people of Northern European descent and may not represent the majority of the MUTYH variants found in people of other ethnicities. The test report does not describe a person's overall risk of developing any type of cancer, and the absence of a variant tested does not rule out the presence of other variants that may be cancer-related. This test is not a substitute for visits to a healthcare provider for recommended screenings or appropriate follow-up and should not be used to determine any treatments.

Type of Use *(Select one or both, as applicable)*

☐ Prescription Use (Part 21 CFR 801 Subpart D) ☒ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of Safe Medical Devices Act of 1990 and 21 CFR 807.92

The assigned 510(k) number is: K182784

Submitter / Company
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Date Prepared
28 September 2018

5.1 Regulatory Information

Table 5.1 Proposed new device

Type of Submission:	Traditional 510k
Common/Usual Name:	**MUTYH-Associated Polyposis (MAP)**
	23andMe Personal Genome Service (PGS) Genetic Health Risk Report for **MUTYH-Associated Polyposis (MAP)**
Regulation Name:	Cancer Predisposition Risk Assessment System
Regulation Description:	A Cancer Predisposition Risk Assessment System is a qualitative in vitro molecular diagnostic system used for determining predisposition for cancer where the result of the test may lead to prophylactic screening, confirmatory procedures, or treatments that may incur morbidity or mortality to the patient. The test could help to inform conversations with a

	healthcare professional. This assessment system is for over-the-counter use. This device does not determine the person's overall risk of developing any types of cancer. This test is not a substitute for visits to a healthcare provider for recommended screenings or appropriate follow-up and should not be used to determine any treatments. This device does not determine the person's overall risk of developing any types of cancer. This test is not a substitute for visits to a healthcare provider for recommended screenings or appropriate follow-up and should not be used to determine any treatments.
Regulation Number:	21 CFR 866.6090
Product Code:	QAZ
Class	Class II
Predicate Device:	23andMe PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants) authorized on March 6, 2018 under DEN170046

5.2 Intended Use

The 23andMe Personal Genome Service (PGS) uses qualitative genotyping to detect select clinically relevant variants in genomic DNA isolated from human saliva collected from individuals ≥18 years for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for **MUTYH-Associated Polyposis (MAP)**

5.3 Indications for Use

The 23andMe Personal Genome Service (PGS) uses qualitative genotyping to detect select clinically relevant variants in genomic DNA isolated from human saliva collected from individuals ≥18 years with the Oragene Dx model OGD500.001 for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for **MUTYH-Associated Polyposis**. The 23andMe PGS Genetic Health Risk Report for **MUTYH-Associated Polyposis** is indicated for reporting of the Y179C and the G396D variants in the MUTYH gene. The report describes if a person is at increased risk of developing colorectal cancer. The two variants included in this report are most common and best studied in people of Northern European descent and may not represent the majority of the MUTYH variants found in people of other ethnicities. The test report does not describe a person's overall risk of developing any type of cancer, and the absence of a variant tested does not rule out the presence of other variants that may be cancer-related. This test is not a substitute for visits to a healthcare provider for recommended screenings or appropriate follow-up and should not be used to determine any treatments.

5.4. Substantially Equivalent Predicate Device

The core components of the PGS are unchanged from the *de novo* authorization for the predicate device, the PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants) (DEN170046), and also the additional *de novo* Authorizations of the PGS for Carrier Screening Tests for Bloom Syndrome (DEN140044) and PGS Genetic Health Risk Reports (DEN160026), including the saliva collection kit, the reagents and beadchip, the instrumentation, the software, the test processes and procedures. The novel components in this traditional 510(k) submission are only (a) the specific variants to be reported, and (b) the qualitative reporting of risk for **MAP,** as opposed to the BRCA related cancer risks included in DEN170046.

As described in Section 13, the 23andMe Personal Genome Service (PGS) is a currently marketed device with reports for autosomal recessive carrier status, pursuant to DEN140044 (and related exemption), genetic health risk reports authorized as part of DEN160026 (and related exemption) and DEN170046, and features that are not considered part of the medical device (e.g. genetic ancestry and cosmetic traits such as eye or hair color).

The **MAP** report, scientific details, and FAQs were designed and developed in the same format as the predicate device, PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants), and conform to the submission agreements and special controls of the authorization (DEN170046). The **MAP** report is intended for over-the-counter, direct-to-consumer use without prescription or physician order. When a customer purchases the PGS with Health reports, the customer must first opt-in to receive carrier status and genetic health risk reports, including the Genetic Health Risk Report for **MAP**. Customers with positive results are advised to share their results with their healthcare provider. As instructed in predicate device authorization DEN170046, the same healthcare provider limitations are included in the package insert:

- This test is not intended to diagnose a disease, determine medical treatment or other medical intervention, or tell the user anything about their current state of health.
- This test is intended to provide users with their genetic information, which may inform health-related lifestyle decisions and conversations with their doctor or other healthcare professional.
- Any diagnostic or treatment decisions must be based on confirmatory prescription testing and/or other information that you determine to be appropriate for your patient, such as additional clinical testing and other risk factors that may affect individual risk and health care.

Thus, the 23andMe PGS Genetic Health Risk Report for **MAP** is substantially equivalent to the predicate, 23andMe PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants) authorized under DEN170046.

5.5 Device Description

The 23andMe Personal Genome Service (PGS) is an over-the-counter (direct-to-consumer), DNA testing service that provides information and tools for consumers to learn about and explore their DNA.

The 23andMe Personal Genome Service (PGS) is a currently marketed, non-invasive genetic information service that combines qualitative genotyping data covering genetic ancestry, traits, and certain heritable health conditions from a single multiplex assay with descriptive information derived from peer reviewed, published genetic research studies. It is a home use, over-the-counter (direct-to-consumer) DNA testing service intended to provide information and tools for consumers to learn about and explore their DNA.

Customer saliva is self-collected using the Oragene·Dx® Device manufactured by DNA Genotek, Inc. (previously cleared for carrier screening indications under K141410, and the same collection kit used to generate performance data for DEN140044, DEN160026 and DEN170046), which consists of a sealable collection tube containing a stabilizing buffer solution. Once the sample is collected, it is shipped to one of our Clinical Laboratory Improvement Amendments (CLIA) certified laboratories for testing.

DNA is isolated from the saliva and tested in a multiplex assay using a customized genotyping beadchip, reagents and instrumentation manufactured by Illumina. The multiplex assay simultaneously tests for more than 500,000 variants, including those for the previously authorized indications, as well as for the indications proposed herein.

The raw data is generated using Illumina GenomeStudio software, and then sent to 23andMe. The data is then analyzed using the 23andMe's proprietary Coregen software, where a genotype is determined for each tested SNP. The results for certain of these SNPs are used to generate personalized reports for the customer that provide information about the detected genotype.

Personalized reports are generated for each user that provide results of the testing performed. These reports tell the user which variant(s) has/have been detected in their sample and provide information on the risk of disease associated with the variant(s). If no variant was detected, that information is also provided. The personalized reports are designed to present scientific concepts to users in an easy-to-understand format. The reports provide scientifically valid information about the risks associated with the presence of a particular variant. The reports are designed to help users understand the meaning of their results and any appropriate actions that may be taken based on their results.

The novel components in this traditional 510(k) submission are only (a) the variants to be reported, and (b) the qualitative reporting of risk for **MAP**.

Engineering drawings, schematics, etc. of the **MAP** report are not applicable to this device.

5.6 Technological Characteristics

Test Type: Qualitative genetic test for single nucleotide polymorphism detection.
Sample Type: Genomic DNA obtained from a human saliva sample.
Target of detection: Single-nucleotide polymorphism.
DNA extraction: Automated and manual methods.
Gene: MUTYH

Variants: Y179C and G396D variants in the MUTYH gene
SNPs: rs34612342 and rs36053993
Genotyping principle: The DNA is fragmented and captured on a bead array by hybridization to immobilized SNP-specific primers, followed by extension with hapten-labeled nucleotides. The primers hybridize adjacent to the SNPs and are extended with a single nucleotide corresponding to the SNP allele. The incorporated hapten-modified nucleotides are detected by adding fluorescently labeled antibodies in several steps to amplify the signals. Data analysis is performed using scatter plots.
Instrument: Illumina iScan and GenomeStudio system.
Assay results: The genotype content is separated, analyzed, and then integrated into pre-defined report templates specific for each condition associated with each genotype.

Table 5.2 Substantial Equivalence

	Predicate BRCA1/BRCA2 (Selected Variants) DEN170046	**Proposed MUTYH-Associated Polyposis (MAP)**	**Similarities and Differences**
Intended Use	The 23andMe Personal Genome Service (PGS) uses qualitative genotyping to detect select clinically relevant variants in genomic DNA isolated from human saliva collected from individuals ≥18 years with the Oragene Dx model OGD500.001 for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants).	The 23andMe Personal Genome Service (PGS) uses qualitative genotyping to detect select clinically relevant variants in genomic DNA isolated from human saliva collected from individuals ≥18 years for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for **MUTYH-Associated Polyposis (MAP)**.	Same PGS product with the addition of 2 new variants in the MUTYH gene.
Indications for Use	The 23andMe PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants) is indicated for reporting of the 185delAG and 5382insC variants in the BRCA1 gene and the 6174delT variant in the BRCA2 gene. The report	The 23andMe Personal Genome Service (PGS) uses qualitative genotyping to detect select clinically relevant variants in genomic DNA isolated from human saliva collected from individuals ≥18 years with the Oragene Dx model	Same PGS product with the addition of 2 new variants in the MUTYH gene.

	describes if a woman is at increased risk of developing breast and ovarian cancer, and if a man is at increased risk of developing breast cancer or may be at increased risk of developing prostate cancer. The three variants included in this report are most common in people of Ashkenazi Jewish descent and do not represent the majority of BRCA1/BRCA2 variants in the general population. The report does not describe a person's overall risk of developing any type of cancer, and the absence of a variant tested does not rule out the presence of other variants that may be cancer-related. This test is not a substitute for visits to a healthcare provider for recommended screenings or appropriate follow-up and should not be used to determine any treatments.	OGD500.001 for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for **MUTYH-Associated Polyposis**. The 23andMe PGS Genetic Health Risk Report for MUTYH-Associated Polyposis is indicated for reporting of the Y179C and the G396D variants in the MUTYH gene. The report describes if a person is at increased risk of developing colorectal cancer. The two variants included in this report are most common and best studied in people of Northern European descent and may not represent the majority of the MUTYH variants found in people of other ethnicities. The test report does not describe a person's overall risk of developing any type of cancer, and the absence of a variant tested does not rule out the presence of other variants that may be cancer-related. This test is not a substitute for visits to a healthcare provider for recommended screenings or appropriate follow-up and should not be used to determine any treatments.	
Collection Kit	Oragene·Dx® saliva collection device (OGD-500.001)	Oragene·Dx® saliva collection device (OGD-500.001)	Same

	K141410	K141410	
Reagents	Illumina Infinium HTS Assay Reagents	Illumina Infinium HTS Assay Reagents	Same
BeadChip	Illumina Infinium BeadChip genotyping chip customized for the PGS. The chip is designed to detect specific single nucleotide polymorphisms (SNPs) as well as other genetic variants; all markers refer to specific positions in the National Center for Biotechnology Information (NCBI) reference human genome.	Illumina Infinium BeadChip genotyping chip customized for the PGS. The chip is designed to detect specific single nucleotide polymorphisms (SNPs) as well as other genetic variants; all markers refer to specific positions in the National Center for Biotechnology Information (NCBI) reference human genome.	Same
Beadpool	Customized for 23andMe	Customized for 23andMe	Same
Instruments	Tecan Evo Illumina iScan	Tecan Evo Illumina iScan	Same
Software	Genome Studio Coregen	Genome Studio Coregen	Same
Sample Matrix	Saliva	Saliva	Same
Method Comparison	100% PPA and NPA for all genotypes	>99% PPA and NPA for all genotypes	Same
Precision	100% reproducibility and 100% repeatability	100% reproducibility and 100% repeatability	Same
Minimum DNA Input	5ng/uL	5ng/uL	Same

5.7 Performance Testing Summary

5.7.1 Method Comparison (Accuracy)

23andMe performed a Method Comparison study to assess the accuracy of the 23andMe BeadChip assay. The goal of the study was to show equivalent genotype assignment between the 23andMe BeadChip assay and Sanger bi-directional DNA sequencing. Saliva samples were selected from the 23andMe customer biobank, based on their pre-determined BeadChip genotype and minimum volume required for testing. All BeadChip genotyping was performed at an independent laboratory site. All chosen samples were then sequenced using Sanger bi-directional sequencing. Genotyping results were compared between BeadChip and sequencing to calculate positive percent agreement (PPA) and negative percent agreement (NPA), with the sequencing results considered to be "truth." The passing criteria were a minimum of 99% PPA and NPA for each SNP. This method comparison study yielded >99% PPA and NPA for all genotypes. Therefore, the study passed the acceptance criteria of at least 99% PPA and NPA.

5.7.2 Precision/Reproducibility

23andMe performed a precision study to determine the reproducibility of the 23andMe BeadChip assay. This study included all G3696 variants, and Y179C common homozygous and heterozygous variants. The goal of the study was to evaluate the following precision parameters of the assay: intra-assay, inter-lot, inter-instrument, inter-operator, inter-day, and inter-lab differences. DNA samples were either commercially available samples or samples that were available in the 23andMe biobank, and were further selected based on their confirmed genotypes. To confirm, each sample was sequenced by bi-directional Sanger sequencing. The same samples were genotyped by the BeadChip assay in a blinded fashion, with 3 lots of reagents, by multiple operator teams per day, using 3 different serial numbers of each of 2 instruments (Tecan and iScan), over 3 days, at each of 2 laboratory sites. BeadChip genotypes were compared with sequenced genotypes to determine the rates of correct BeadChip genotype calls.

This precision study yielded 100% correct genotype calls for all samples across multiple days, operator teams, instruments, and reagent lots at two independent laboratory sites. Therefore, the study passed the acceptance criteria of at least 99% correct calls at each of the two laboratory sites. There was no variation between any study conditions or any replicates for a given sample. Therefore, the study demonstrated 100% reproducibility and 100% repeatability for a given sample. Therefore, the study had 100% reproducibility and 100% repeatability.

5.7.3 DNA Input

23andMe performed a DNA input study for the 23andMe PGS multiplex assay. This study included all G3696 variants, and Y179C common homozygous and heterozygous variants. Due to the rarity of this sample type, the study excluded the Y179C rare homozygous variant.

The design of the study was consistent with our previous agreement recorded in Q160823-A001 meeting minutes dated August 9, 2016. The goal of the study was to confirm that the previously determined minimum concentration claim of 5ng/uL of DNA is necessary for successful assignment of the correct genotype using the 23andMe PGS assay. The DNA requirement for the PGS is defined as the lowest DNA concentration at which at least 95% of samples yielded the correct call. DNA samples were obtained from commercial sources or obtained from the 23andMe biobank based on their listed genotypes. Each sample was diluted to 3 different DNA

concentrations and genotyped in a blinded fashion using 3 lots of reagents. To confirm the genotype call, each sample was also sequenced using bi-directional Sanger sequencing. Genotype calls from the PGS assay were compared with sequenced genotypes to determine the rates of correct genotype calls at each DNA concentration.

This study yielded 100% correct genotype calls for all samples and all reagent lots tested at sample DNA concentrations of 5, 15, and 50 ng/µL. Therefore, the study passed the acceptance criteria of 95% correct calls at a sample DNA concentration of 5 ng/µL. This study demonstrates that the PGS tests are valid for samples with a DNA concentration range of 5 ng/µL to 50 ng/µL. The performance requirement specified by contracted laboratory SOPs, is conservatively set at a minimum DNA requirement of 15 ng/µL.

5.7.4 Interfering Substance (Specificity)

The PGS requires the use of an FDA-cleared collection device (K141410). The device used for the test is the exact same device used for all carrier screening reports (DEN140044) and all genetic health risk reports (DEN160026 & DEN170046). A test for potentially interfering mutations was performed in support of DEN140044, and no new interfering substances have been identified. The cleared device includes instructions for use instructing the user to not eat, drink, smoke or chew gum for 30 minutes prior to collecting their saliva, thus minimizing the availability of interferents in the sample. 23andMe performed a series of studies to assess the effects of endogenous substances, exogenous substances, microbial substances, and smoking on the 23andMe PGS assay in support of submission DEN140044. Over these four studies, more than 35,000 sample replicates were tested, with no discordant or No Call results across 99 SNPs, for an accuracy of 100% when following the instructions for use (i.e., nothing by mouth for at least 30 minutes prior to collecting saliva).

5.7.5 Potentially Interfering Mutations

23andMe has identified three (3) potentially interfering mutations near Y179C, and four (4) potentially interfering mutations near G396D that are within the binding region of the probes for the variants of interest. The Company was unable to identify commercially available samples for these potentially interfering mutations, therefore has added a statement in the limitations section of the package insert stating that the impact of interfering mutations has not been evaluated.

5.7.6 Matrix Comparison

Human saliva is the only suitable sample matrix, therefore Matrix Comparison studies are not applicable.

5.7.7 Shelf Life

The PGS requires the use of the same FDA-cleared collection device that was reviewed and cleared in submission K141410. Shelf life data, summarized below, was previously reviewed and authorized in K141410, DEN140044, DEN160026, and DEN170046.

Pre-collection shelf-life conditions were evaluated by storing unused Oragene·Dx® devices at room temperature, 6°C ± 4°C or -20°C ± 5°C for up to 24 months. Devices were exposed to

multiple freeze/thaw cycles of -20°C ± 5°C/50°C ± 5°C. In a separate study, devices were sent by standard mail to donors for collection and the donors mailed their samples directly to the processing laboratories. At all study time points a subset of devices were evaluated for physical and chemical properties to ensure the product specifications remained within acceptable tolerances. Another subset of devices was used to collect saliva from which DNA was extracted and analyzed for yield and A260/A280 ratio. The data supports shelf-life claims of room temperature storage for up to 24 months. Additionally, the devices may be transported by standard mail at temperatures ranging from -20°C ± 5°C to 50°C ± 5°C.

Post-collection sample stability of the Oragene·Dx® device was evaluated by having 30 donors each self- collect saliva samples using Oragene·Dx® OGD-500. Samples were stored at room temperature, 6°C ± 4°C or -20°C ± 5°C for 12 months or at 50°C ± 5°C for 3 months. At all study time-points, DNA was extracted and analyzed for yield and A260/A280 ratio. Samples stored at room temperature were analyzed for microbial content using a real-time PCR-based assay. The data supports post-collection storage at -20°C to room temperature for up to 12 months and at 50°C ± 5°C for 3 months.

5.7.8 Clinical Performance

The clinical sensitivity and specificity are estimated based on published studies of variant frequencies in various populations and the results of analytical studies reported in this submission, as well as allele frequencies in the 23andMe customer base for the genetic variants and associations included in this submission.

The following table summarizes the clinical performance data for the PGS Genetic Health Risk Report for **MAP**.

Table 5.3 Clinical Performance

Allele Frequencies (%): in the 23andMe Database[a], ExAc database, and from published literature[b]

Ancestry group	Y179C		G396D	
	23andMe	Published	23andMe	Published
European	0.21%	0.25%[c] 0.20%[d]	0.58%	0.40%[c] 0.40%[d]
African American	0.06%	0.05%[e]	0.21%	0.11%[e]
Ashkenazi Jewish	0.00%	Unknown	0.00%	Unknown
East Asian	0.00%	0.00% 0.00%[f]	0.01%	0.01% 0.00%[f]
Hispanic/Latino	0.14%	0.10%	0.51%	0.33%

South Asian	0.03%	0.00%	0.03%	0.02%

[a] Based on approximately 872,000 individuals with European ancestry, 47,500 individuals with African-American ancestry, 38,500 individuals with Ashkenazi Jewish ancestry, 35,000 individuals with East Asian ancestry, 123,500 individuals with Hispanic/Latino ancestry, and 10,000 individuals with South Asian ancestry. Because of the privacy considerations surrounding the use of customer data (namely, the risk of exposing the identity of individuals in the database), the frequencies provided are rounded to a hundredth of a percent and truncated at a minimum frequency if the number of individuals with a variant is fewer than five.
[b] Unless a reference is specified, the data was extracted from ExAc database: http://exac.broadinstitute.org/ accessed 18Jun2018.
[c] European (Non-Finnish)
[d] Poulsen and Bisgaard 2008, data from USA population
[e] African
[f] Poulsen and Bisgaard 2008, data from Japanese population

5.7.9 Labeling Comprehension

The comprehension of key report concepts were determined to be the same as those identified and previously tested in the predicate device label comprehension study (DEN170046). The average comprehension rate per comprehension concept ranged from 90.7% to 96.1%, therefore the comprehension study met the predefined acceptance criteria of 90% or greater overall comprehension.
The representative Genetic Health Risk reports and supporting educational materials were effective in communicating relevant concepts to users unfamiliar with genetic testing sufficient for the safe use of the PGS Genetic Health Risk Report for **MAP**.

5.8. Discussion

The PGS Genetic Health Risk Report for **MAP** has a similar intended use as the predicate, is not technologically different than the predicate, and therefore presents no new issues of safety or effectiveness when compared to the previously authorized predicate device (DEN170046). Specifically, this submission for the PGS Genetic Health Risk Report for **MAP** provides analytical and clinical data demonstrating that the PGS Test generates an accurate result, and that the user can adequately interpret the result for both of the variants.

5.9. Conclusion

The PGS Genetic Health Risk Report for **MAP** is substantially equivalent to the predicate device DEN170046 (23andMe PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants), authorized March 6, 2018). As presented, the PGS Genetic Health Risk Report for **MAP** is a safe and effective consumer product that can safely and effectively assist and encourage women and men with positive results to engage in potentially life saving conversations with their healthcare provider.