January 06, 2022

23andMe, Inc.
Marianna Frendo
Manager, Regulatory Affairs
349 Oyster Point Blvd.
South San Francisco, CA 94080

Re: K211499
Trade/Device Name: 23andMe PGS Genetic Risk Report for Hereditary Prostate Cancer (HOXB13-Related)
Regulation Number: 21 CFR 866.6090
Regulation Name: Cancer Predisposition Risk Assessment System
Regulatory Class: Class II
Product Code: QAZ
Dated: May 12, 2021
Received: May 14, 2021

Dear Marianna Frendo:

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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Soma Ghosh, Ph.D.
Chief
Molecular Pathology and Cytology Branch
Division of Molecular Genetics
and Pathology
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K211499

Device Name
23andMe Personal Genome Service (PGS) Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related)

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 for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related). The 23andMe PGS Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13- Related) is indicated for reporting of the G84E variant in the HOXB13 gene. The report describes if a person has the G84E variant and if a male is at increased risk for prostate cancer. The variant included in this report is most common in people of European descent. 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 for diagnosis, to determine any treatments or medical interventions.

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

SUBMITTER / PRIMARY COMPANY
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Establishment Registration Number: 3007699459
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5.1. REGULATORY INFORMATION

Table 5.1 Proposed new device

Type of Submission:	Traditional 510k
Common/Usual Name:	Hereditary Prostate Cancer (HOXB13-Related)
Trade/proprietary Name:	23andMe Personal Genome Service (PGS) Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related)
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.
Regulation Number:	21 CFR §866.6090
Product Code:	QAZ
Class	Class II

5.2. LEGALLY MARKETED EXISTING DEVICE

Trade Name: 23andMe Personal Genome Service (PGS)				
Report Type	Carrier Status Reports	Genetic Health Risk Reports	Genetic Health Risk Reports	Pharmacogenetic Reports
Classification Name	Autosomal Recessive Carrier Screening Gene Mutation Detection System	Genetic Variant Detection and Health Risk Assessment System	Cancer Predisposition Risk Assessment System	Direct-to-Consumer Access Pharmacogenetic Assessment System
Classification Panel	Immunology / Clinical Chemistry	Immunology/ Hematology	Molecular Genetics/ Pathology	Molecular Genetics/ Clinical Chemistry
Regulation Number	21 CFR §866.5940	21 CFR §866.5950	21 CFR §866.6090	21 CFR §862.3364
Device Class	Class II	Class II	Class II	Class II
510(k)	Exempt	Exempt	Required	Required
Product Code	PKB	PTA	QAZ	QDJ
DEN/510(k) number	DEN140044	DEN160026	DEN170046, K182784	DEN180028, K193492
Decision Date(s)	19Feb2015	06Apr2017	06Mar2018, 18Jan2019	31Oct2018, 17Aug2020

5.3. LEGALLY MARKETED PREDICATE DEVICE(S)

23andMe Personal Genome Service (PGS)		
Predicate	#1	#2
Report Name	Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants)	Genetic Health Risk Report for MUTYH-Associated Polyposis (MAP)
Classification Name	Cancer Predisposition Risk Assessment System	Cancer Predisposition Risk Assessment System
Classification Panel	Molecular Genetics/ Pathology	Molecular Genetics/ Pathology
Regulation Number	21 CFR §866.6090	21 CFR §866.6090
Device Class	Class II	Class II
Product Code	QAZ	QAZ
DEN/510(k) number	DEN170046	K182784
Decision Date(s)	06Mar2018	18Jan2019

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, DEN170046, K182784, DEN180028, and K193492, 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, and off the shelf 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.

Raw data is generated using Illumina GenomeStudio software, and then sent to 23andMe. The data is then analyzed using 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 genetic health risk variant(s) have been detected in their sample and provide information about the 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 modified components of the Personal Genome Service included in this 510(k) submission are new labeling to include (a) one new variant to be reported, and (b) the qualitative reporting of one's Genetic Health Risk for Hereditary Prostate Cancer (HOXB13-Related).

Engineering drawings, schematics, etc. of Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related) are not applicable to this device.

5.6. 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 for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related). The 23andMe PGS Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13- Related) is indicated for reporting of the G84E variant in the HOXB13 gene. The report describes if a person has the G84E variant and if a male is at increased risk for prostate cancer. The variant included in this report is most common in people of European descent. 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 for diagnosis, to determine any treatments or medical interventions.

5.7. COMPARISON TO SUBSTANTIALLY EQUIVALENT PREDICATE DEVICES

5.7.1 Intended use / Indications for use

	BRCA1/BRCA2 (Selected Variants) DEN170046	**MUTYH Associated Polyposis K182784**	**Hereditary Prostate Cancer (HOXB13-Related)**	**Similarities and differences**
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 BRCA1/BRCA2 (Selected Variants) The 23andMe PGS Genetic Health Risk Report for	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	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 Hereditary Prostate Cancer (HOXB13-Related). The 23andMe PGS Genetic Health Risk Report for	Similar.

	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 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 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	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 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	Hereditary Prostate Cancer (HOXB13-Related) is indicated for reporting of the G84E variant in the HOXB13 gene. The report describes if a person has the G84E variant and if a male is at increased risk for prostate cancer. The variant included in this report is most common in people of European descent. 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 for diagnosis, to determine any treatments or	

	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.	appropriate follow-up and should not be used to determine any treatments.	medical interventions.	

5.7.2 Technological Characteristics

	BRCA1/BRCA2 (Selected Variants) DEN170046	**MUTYH Associated Polyposis k182784**	**Hereditary Prostate Cancer (HOXB13-Related)**	**Similarities and differences**
Technological Characteristics				
Test Type	Qualitative genetic test for single nucleotide polymorphism detection	Qualitative genetic test for single nucleotide polymorphism detection	Qualitative genetic test for single nucleotide polymorphism detection	Same
Sample Type/Matrix	Genomic DNA obtained from a human saliva sample	Genomic DNA obtained from a human saliva sample	Genomic DNA obtained from a human saliva sample	Same
Gene	BRCA1 and BRCA2	MUTYH	HOXB13	Different
Variant	185delAG and 5382insC variants in the BRCA1 gene, and the 6174delT variant	Y179C and G396D	G84E	Different

	in the BRCA2 gene			
SNP	i4000377, i4000378, and i4000379	rs34612342 and rs36053993	rs138213197	Different
Genotyping Principle	DNA is fragmented and captured on a beadchip array by hybridization to immobilized SNP-specific primers, followed by extension with hapten-labeled nucleotides. 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	DNA is fragmented and captured on a beadchip array by hybridization to immobilized SNP-specific primers, followed by extension with hapten-labeled nucleotides. 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	DNA is fragmented and captured on a beadchip array by hybridization to immobilized SNP-specific primers, followed by extension with hapten-labeled nucleotides. 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	Same
Assay Components and instruments				
Collection kit	Oragene·Dx®	Oragene·Dx®	Oragene·Dx®	Same

	saliva collection device (OGD-500.001) K141410	saliva collection device (OGD-500.001) K141410	saliva collection device (OGD-500.001) K141410	
Reagents	Illumina Infinium HTS assay Reagents	Illumina Infinium HTS assay Reagents	Illumina Infinium HTS assay Reagents	Same
Beadchip	Illumina Infinium Array customized for the PGS. The beadchip array 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 Array customized for the PGS. The beadchip array 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 Array customized for the PGS. The beadchip array 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
Instruments	Tecan Evo Illumina iScan with GenomeStudio Software	Tecan Evo Illumina iScan with GenomeStudio Software	Tecan Evo Illumina iScan with GenomeStudio Software	Same
Software	Coregen	Coregen	Coregen	Same
Performance				
Accuracy / Method Comparison	>99% PPA and NPA for all genotypes	>99% PPA and NPA for all genotypes	>99% PPA and NPA for all genotypes	Same

Precision	>99% reproducibility and >99% repeatability	>99% reproducibility and >99% repeatability	>99% reproducibility and >99% repeatability	Same
Minimum DNA Input	5ng/uL	5ng/uL	5ng/uL	Same
Interfering Substance	100% accuracy when following the instructions for use	100% accuracy when following the instructions for use	100% accuracy when following the instructions for use	Same
Potentially Interfering Mutations	Warnings and Limitations: The performance of these tests may be affected by the presence of rare mutations. The impact of potentially interfering mutations has not been evaluated	Warnings and Limitations: The performance of these tests may be affected by the presence of rare mutations. The impact of potentially interfering mutations has not been evaluated	Warnings and Limitations: The performance of these tests may be affected by the presence of rare mutations. The impact of potentially interfering mutations has not been evaluated	Same
Matrix Comparison	Human Saliva Only	Human Saliva Only	Human Saliva Only	Same
Stability	Specimen: 8 years Reagents: 6-12 Months Collection Kit: 24 months	Specimen: 8 years Reagents: 6-12 Months Collection Kit: 24 months	Specimen: 8 years Reagents: 6-12 Months Collection Kit: 24 months	Same
Labeling Comprehension	90% or greater overall comprehension rate	90% or greater overall comprehension rate	90% or greater overall comprehension rate	Same

5.8. PERFORMANCE TESTING SUMMARY

All performance testing is managed by our ISO 13485:2016 certified Quality Management System, and conforms to design control requirements specified in 21CFR §820.30.

Analytical and Comprehension studies were performed and documented as described in Special Controls published in reclassification order DEN170046.

Software Verification and Validation studies were performed and documented as described in Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices issued on 11May2005. 23andMe employs a variety of administrative, technical, and physical safeguards in order to efficiently mitigate cybersecurity risks. 23andMe has been certified for compliance with ISO/IEC 27001:2013 Information Security Management System, including control implementation guidance within ISO/IEC 27018:2019 as well as the requirements and control implementation guidance within ISO/IEC 27701:2019 as a data controller. 23andMe is also actively implementing the controls and policies as defined in the “HITRUST CSF” (Common Security Framework), which includes the FDA recommended NIST Cybersecurity Framework (CsF).

5.8.1 Method Comparison (Accuracy)

23andMe performed a Method Comparison study to assess the accuracy of the 23andMe assay. The goal of the study was to show equivalent genotype assignment between the 23andMe assay and Sanger bi-directional DNA sequencing. Saliva samples were selected from the 23andMe customer biobank, based on their predetermined genotype and minimum volume required for testing. All assay genotyping was performed at approved contract laboratory sites. All chosen samples were then sequenced using Sanger bi-directional sequencing by an approved supplier. Genotyping results were compared between genotyping assay and bi-directional 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.

5.8.2 Precision / Reproducibility

23andMe performed a precision study to determine the reproducibility of the 23andMe assay. 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 selected based on their confirmed genotypes, and were obtained from the 23andMe biobank. To confirm, each sample was sequenced by bi-directional Sanger sequencing. The same samples were genotyped by the 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. Assay genotypes were compared with sequenced genotypes to determine the rates of correct 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.

5.8.3 DNA Input

23andMe performed a DNA input study for the genotyping assay. 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 determine the lowest concentration of DNA that is necessary for successful assignment of the correct genotype. 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 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 results 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 assay can correctly genotype 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.

5.8.4 Interfering Substance (Specificity)

The PGS assay 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 labeling in the form of a package insert instructing the user to not eat, drink, smoke or chew gum for 30 minutes prior to collecting their saliva, thus minimizing the availability of potentially interfering substances in the saliva sample. 23andMe performed a series of studies to assess the effects of endogenous substances, exogenous substances, microbial substances, and smoking on the 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).

5.8.5 Potentially Interfering Mutations

23andMe has identified one(1) potentially interfering mutation near G84E. The Company was unable to identify commercially available samples for these potentially interfering mutations.

Therefore, a statement has been added to the limitations section of the package insert stating that the impact of interfering mutations has not been evaluated.

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

5.8.7 Shelf life:
The PGS requires the use of the same FDA-cleared collection device and reagents that have been previously reviewed and authorized in K141410 and DEN140044.

5.8.8 Clinical Performance:
Clinical performance is 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 database 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 Hereditary Prostate Cancer (HOXB13-Related).

Table 5.3 Clinical Performance
HOXB13 G84E Allele Frequencies (%) in the 23andMe database[a] and the gnomAD database[b]

Ancestry group	23andMe	gnomAD
European	0.18%	0.76%[c] 0.24%[d]
African American	0.04%	0.04%
Ashkenazi Jewish	<0.01%	0.01%
East Asian	0.00%	0.00%
Hispanic/Latino	0.06%	0.003%
South Asian	0.00%	0.00%
Middle Eastern	<0.01%	n/a

[a] Based on approximately 5,552,000 individuals with European ancestry, 303,000 individuals with African American ancestry, 168,000 individuals with Ashkenazi Jewish ancestry, 235,000 individuals with East Asian ancestry, 957,000 individuals with Hispanic/Latino ancestry, 57,000 individuals with South Asian ancestry, and 60,000 individuals with Middle Eastern 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] Data was extracted from the gnomAD database: https://gnomad.broadinstitute.org/ accessed 09May2020.
[c] European (Finnish)

[d] European (Non-Finnish)

5.8.9 Labeling Comprehension

The key report message concepts for the Hereditary Prostate Cancer (HOXB13-Related) test were reviewed and determined to be the same as those identified and previously tested in the Genetic Health Risk device label comprehension study (DEN160026), which was determined suitable for the predicate devices (DEN170046 and K182784). 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 content 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 Hereditary Prostate Cancer (HOXB13-Related).

5.9. DISCUSSION

The PGS Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related) has a similar intended use as the predicate devices, is not technologically different than the predicate devices, and therefore presents no new issues of safety or effectiveness when compared to the previously authorized predicate devices (DEN170046, K182784). Specifically, this submission for the PGS Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related) includes analytical and clinical data demonstrating that the assay generates accurate results which the user can appropriately interpret.

5.10. CONCLUSION

The PGS Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related) is substantially equivalent to the predicate devices DEN170046 (23andMe PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants), authorized March 6, 2018) and K182784 (23andMe PGS Genetic Health Risk Report for MUTYH Associated Polyposis cleared on January 18, 2019). As presented, the PGS Genetic Health Risk Report for Hereditary Prostate Cancer (HOXB13-Related) 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.