October 27, 2022

Progenika Biopharma S.A., a Grifols company
Diego Tejedor
Technical Director
Ibaizabal bidea, Edificio 504, Parque Tecnológico de Bizkaia
Derio, Bizkaia 48160
Spain

Re: K221420
Trade/Device Name: AlphaID At Home Genetic Health Risk Service
Regulation Number: 21 CFR 866.5950
Regulation Name: Genetic health risk assessment system
Regulatory Class: Class II
Product Code: PTA
Dated: September 30, 2022
Received: October 6, 2022

Dear Diego Tejedor:

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,

Ying Mao, Ph.D.
Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
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)*
K221420

Device Name
AlphaID™ At Home Genetic Health Risk Service

Indications for Use *(Describe)*
The AlphaID™ At Home Genetic Health Risk Service uses qualitative genotyping to detect clinically relevant genetic variants associated with alpha-1 antitrypsin deficiency (AATD) in genomic DNA isolated from human saliva collected from individuals ≥ 18 years with ORAcollect·Dx OCD-100.014 for the purpose of reporting and interpreting Genetic Health Risks (GHR).
This Service is indicated for reporting 14 genetic variants in the SERPINA1 gene: PI*S; PI*Z; PI*I; PI*M procida; PI*M malton; PI*S iiyama; PI*Q0 granite falls; PI*Q0 west; PI*Q0 bellingham; PI*F; PI*P lowell; PI*Q0 mattawa; PI*Q0 clayton, and PI*M heerlen. The report describes if a person is at an increased risk of developing either lung and/or liver disease linked to AATD. The report does not describe a person´s overall risk of developing lung and/or liver disease. AATD is more common in persons of European descent.

Special conditions for use statements:
a. For over-the-counter (OTC) use.
b. The test is intended for users ≥18 years old.
c. The test is not a substitute for an appointment with a healthcare professional. It is recommended that the user consults with a healthcare professional if the user has any questions or concerns about his/her results.
d. The test does not diagnose a disease or condition, determine medical treatment or other medical intervention, or tell the user anything about their current state of health. Only a healthcare professional can diagnose a disease or condition.
e. Any diagnostic or treatment decisions must be based on confirmatory prescription testing and/or other information that a healthcare professional determines to be appropriate for the patient, such as additional clinical testing and other risk factors that may affect individual risk and health care.
f. The test detects 14 variants in the SERPINA1 gene linked to AATD. These 14 variants explain 95% of AATD cases. The absence of a variant tested does not rule out the presence of other genetic variants that may be disease-related.
g. The test does not describe a person's overall risk of developing AATD. In addition, other genetic and all non-genetic factors should be considered
h. The laboratory may be unable to process every user's sample. The probability that the laboratory cannot process a sample can be up to 0.5%. If this happens, the user will receive an email notification. The user will also receive another AlphaID™ At Home Saliva Collection Kit to provide a new sample to the laboratory.
i. The user´s race, ethnicity, age and sex may affect how the genetic results are interpreted.
j. Subject to meeting limitations contained in the special controls under the regulation 21 CFR 866.5950.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

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Office of Chief Information Officer
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510(K) SUMMARY

A. GENERAL INFORMATION

Submission Date: May 6, 2022

Submitter Information:

Submitted By:

Progenika Biopharma S.A.
Parque Tecnológico de Bizkaia
Ibaizabal bidea, Edificio 504
C.P. 48160, Derio – Bizkaia (Spain)
Telephone number: +34 94 406 45 25
Fax number: +34 94 406 45 26

Contact Person:

Diego Tejedor
Technical Director, Progenika Biopharma S.A.
diego.tejedor@grifols.com

B. PURPOSE FOR SUBMISSION

To obtain a substantial equivalence determination for AlphaID™ At Home Genetic Health Risk Service

C. MEASURAND

14 genetic variants in the *SERPINA1* gene: PI*S; PI*Z; PI*I; PI*M procida; PI*M malton; PI*S iiyama; PI*Q0 granite falls; PI*Q0 west; PI*Q0 bellingham; PI*F; PI*P lowell; PI*Q0 mattawa; PI*Q0 clayton, and PI*M heerlen.

D. TYPE OF TEST

Qualitative in vitro molecular diagnostic system.

E. APPLICANT

Progenika Biopharma S.A.

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F. PROPRIETARY AND ESTABLISHED NAMES

AlphaID™ At Home Genetic Health Risk Service.

G. REGULATORY INFORMATION

Trade Name:	AlphaID™ At Home Genetic Health Risk Service
Classification:	Class II (Special Controls)
Regulation:	21 CFR 866.5950
Regulation Name:	Genetic Health Risk Assessment System
Product Code:	PTA
Panel:	Immunology

H. INTENDED USE

See Indications for Use below.

I. INDICATIONS FOR USE

1. Indications for Use:

   The AlphaID™ At Home Genetic Health Risk Service uses qualitative genotyping to detect clinically relevant genetic variants associated with alpha-1 antitrypsin deficiency (AATD) in genomic DNA isolated from human saliva collected from individuals ≥ 18 years with ORAcollect·Dx OCD-100.014 for the purpose of reporting and interpreting Genetic Health Risks (GHR).

   This Service is indicated for reporting 14 genetic variants in the *SERPINA1* gene: PI*S; PI*Z; PI*I; PI*M procida; PI*M malton; PI*S iiyama; PI*Q0 granite falls; PI*Q0 west; PI*Q0 bellingham; PI*F; PI*P lowell; PI*Q0 mattawa; PI*Q0 clayton, and PI*M heerlen. The report describes if a person is at an increased risk of developing either lung and/or liver disease linked to AATD. The report does not describe a person´s overall risk of developing lung and/or liver disease. AATD is more common in persons of European descent.

2. Special Conditions for Use Statements:

   a. For over-the-counter (OTC) use.
   b. The test is intended for users ≥18 years old.
   c. The test is not a substitute for an appointment with a healthcare professional. It is recommended that the user consults with a healthcare professional if the user has any questions or concerns about his/her results.
   d. The test does not diagnose a disease or condition, determine medical

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treatment or other medical intervention, or tell the user anything about their current state of health. Only a healthcare professional can diagnose a disease or condition.

e. Any diagnostic or treatment decisions must be based on confirmatory prescription testing and/or other information that a healthcare professional determines to be appropriate for the patient, such as additional clinical testing and other risk factors that may affect individual risk and health care.

f. The test detects 14 variants in the *SERPINA1* gene linked to AATD. These 14 variants explain 95% of AATD cases. The absence of a variant tested does not rule out the presence of other genetic variants that may be disease-related.

g. The test does not describe a person's overall risk of developing AATD. In addition, other genetic and all non-genetic factors should be considered

h. The laboratory may be unable to process every user's sample. The probability that the laboratory cannot process a sample can be up to 0.5%. If this happens, the user will receive an email notification. The user will also receive another AlphaID™ At Home Saliva Collection Kit to provide a new sample to the laboratory.

i. The user´s race, ethnicity, age and sex may affect how the genetic results are interpreted.

j. Subject to meeting limitations contained in the special controls under the regulation 21 CFR 866.5950

3. Special Instrument Requirements:

The A1AT Genotyping Test Kit used for detection and identification of 14 allelic variants and their associated alleles found in the A1AT codifying gene *SERPINA1* is to be used with the Luminex 200™ instrument (with xPONENT® software).

Raw data from the Luminex System (csv. files containing the MFI value for each bead type) is processed with the A1AT Genotyping Test ANALYSIS SOFTWARE to provide allelic variant genotypes, which are subsequently converted into associated alleles, based on current scientific evidence. Additionally, the software application also provides the type of Genetic Health Risk Report associated with the identified alleles, which is subsequently used as the basis for the generation of personalized reports by the AlphaID™ At Home Genetic Health Risk Service website and result portal (AlphaID System).

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Depending on the specific variant combination detected, the AlphaID™ At Home Genetic Health Risk Service provides the individuals' genetic health risk for developing lung and liver disease linked to AATD.

J. DEVICE DESCRIPTION

The AlphaID™ At Home Genetic Health Risk Service (AlphaID At Home) uses qualitative genotyping to detect clinically relevant genetic variants associated with alpha1-antitrypsin deficiency (AATD) and provides a report describing if a person is at risk of developing either lung and/or liver disease linked to AATD. This Service is direct-to-consumer and intended for an Over-the Counter (OTC) use.

The AlphaID™ At Home Genetic Health Risk Service is composed by AlphaID™ At Home Saliva Collection kit for human saliva sample collection (ORAcollect®·Dx OCD-100.014), A1AT Genotyping Test for the genetic analysis and detection of genetic variants associated with alpha-1 antitrypsin deficiency (AATD), and AlphaID™ At Home Genetic Health Risk Service website and result portal software to provide the contents and the procedure to order and use the over the counter (OTC) Service.

A consumer's saliva is self-collected using custom version ORAcollect·Dx (model OCD-100.014) device manufactured by DNA Genotek, Inc (See K212745) which consists of collection tube containing a stabilizing buffer solution. Once the sample is collected, it is shipped to Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory for processing.

Human DNA from the saliva sample is isolated and processed with the A1AT Genotyping Test device (K211115) that provides results on 14 genetic variants in the *SERPINA1* gene: PI*S; PI*Z; PI*I; PI*M procida; PI*M malton; PI*S iiyama; PI*Q0 granite falls; PI*Q0 west; PI*Q0 bellingham; PI*F; PI*P lowell; PI*Q0 mattawa; PI*Q0 clayton, and PI*M heerlen.

Briefly, genomic DNA extracted from human saliva is amplified and biotinylated by multiplex PCR and PCR products are denatured and hybridized to oligonucleotide probes coupled to color-coded beads. Hybridized DNA is labeled with a fluorescent conjugate and the resulting signal is detected with a Luminex® 200™ system. Raw fluorescence data is processed with the A1AT Genotyping Test ANALYSIS SOFTWARE to provide allelic variant genotypes, which are subsequently converted into associated alleles, based on current scientific evidence. Additionally, the software application also provides the type of Genetic Health Risk Report associated with the identified alleles, which is subsequently used as the basis for the generation of personalized reports by the AlphaID™ At Home Genetic Health Risk Service website and result portal.

Depending on the specific variant combination detected, the AlphaID™ At Home

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Genetic Health Risk Service provides the individuals' genetic health risk for developing lung and liver disease linked to AATD. Personalized reports, in an easy-to-understand format are generated for each consumer that provide results of the testing performed.

K. SUBSTANTIAL EQUIVALENCE INFORMATION

1. Predicate device name(s):
   23andMe Personal Genome Service (PGS) Genetic Health Risk Test (Alpha-1 Antitrypsin Deficiency)

2. Predicate 510(k) number(s):
   DEN160026

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3. Comparison with predicate:

Table 1: Predicate Device Comparison

Item	Predicate Device: 23andMe Personal Genome Service (PGS) for A1AT (DEN160026/DEN140044)	Candidate Device: AlphaID At Home Genetic Health Risk Service
SIMILARITIES		
Intended use	The 23andMe Personal Genome Service (PGS) Test uses qualitative genotyping to detect the following clinically relevant variants in genomic DNA isolated from human saliva collected from individuals ≥18 years with the Oragene Dx model OGD-500.001 for the purpose of reporting and interpreting Genetic Health Risks (GHR): The 23andMe PGS Genetic Health Risk Report for Alpha-1 Antitrypsin Deficiency is indicated for reporting of the PI*Z and PI*S variants in the *SERPINA1* gene. This report describes if a person has variants associated with AAT deficiency and a higher risk for lung or liver disease, but it does not describe a person's overall risk of developing lung or liver disease. This test is most relevant for people of European descent.	The AlphaID™ At Home Genetic Health Risk Service uses qualitative genotyping to detect clinically relevant genetic variants associated with alpha-1 antitrypsin deficiency (AATD) in genomic DNA isolated from human saliva collected from individuals ≥ 18 years with ORAcollect·Dx OCD-100.014 for the purpose of reporting and interpreting Genetic Health Risks (GHR). This Service is indicated for reporting 14 genetic variants in the *SERPINA1* gene: PI*S; PI*Z; PI*I; PI*M procida; PI*M malton; PI*S iiyama; PI*Q0 granite falls; PI*Q0 west; PI*Q0 bellingham; PI*F; PI*P lowell; PI*Q0 mattawa; PI*Q0 clayton, and PI*M heerlen. The report describes if a person is at an increased risk of developing either lung and/or liver disease linked to AATD. The Service does not describe a person´s overall risk of developing lung and/or liver disease. AATD is more common in persons of European descent.

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Item	Predicate Device: 23andMe Personal Genome Service (PGS) for A1AT (DEN160026/DEN140044)	Candidate Device: AlphaID At Home Genetic Health Risk Service
Special Conditions for Use Statements	a. For over-the-counter (OTC) use. b. This test is not a substitute for visits to a healthcare provider. It is recommended that you consult with a healthcare provider if you have any questions or concerns about your results. c. The 23andMe PGS Genetic Health Risk Tests for Hereditary Thrombophilia, Alpha-1 Antitrypsin Deficiency, Alzheimer's disease, Parkinson's disease, Gaucher Disease, Factor XI Deficiency, Celiac disease, and Glucose-6-Phosphate-Dehydrogenase Deficiency, Early-Onset Primary Dystonia and Hereditary Hemochromatosis do not detect all genetic variants associated with the aforementioned diseases. The absence of a variant tested does not rule out the presence of other genetic variants that may be disease-related. d. The test is intended for users ≥ 18 years old. e. The test does not diagnose any specific health conditions. Results should not be used to make medical decisions. f. The laboratory may not be able to process a user's sample. The probability that the laboratory cannot process a sample can be up to 7.6%. g. A user's race, ethnicity, age, and sex may affect how the genetic test results are interpreted. h. Subject to meeting the limitations contained in the special controls under regulation 21 CFR 866.5950.	a. For over-the-counter (OTC) use. b. The test is intended for users ≥18 years old. c. The test is not a substitute for an appointment with a healthcare professional. It is recommended that the user consults with a healthcare professional if the user has any questions or concerns about his/her results. d. The test does not diagnose a disease or condition, determine medical treatment or other medical intervention, or tell the user anything about their current state of health. Only a healthcare professional can diagnose a disease or condition. e. Any diagnostic or treatment decisions must be based on confirmatory prescription testing and/or other information that a healthcare professional determines to be appropriate for the patient, such as additional clinical testing and other risk factors that may affect individual risk and health care. f. The test detects 14 variants in the *SERPINA1* gene linked to AATD. These 14 variants explain 95% of AATD cases. The absence of a variant tested does not rule out the presence of other genetic variants that may be disease-related. g. The test does not describe a person's overall risk of developing AATD. In addition, other genetic and all non-genetic factors should be considered h. The laboratory may be unable to process every user's sample. The probability that the laboratory cannot process a sample can be up to 0.5%. If this happens, the user will receive an email notification. The user will also receive another AlphaID™ At Home Saliva Collection Kit to provide a new sample to the laboratory. i. The user´s race, ethnicity, age and sex may affect how the genetic results are interpreted. j. Subject to meeting limitations contained in the special controls under the regulation 21 CFR 866.5950

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Item	Predicate Device: 23andMe Personal Genome Service (PGS) for A1AT (DEN160026/DEN140044)	Candidate Device: AlphaID At Home Genetic Health Risk Service
Indications for use	This report describes if a person has variants associated with A1AT deficiency and a higher risk for lung or liver disease, but it does not describe a person's overall risk of developing lung or liver disease	**Same**
Intended use population	Any individual ≥18 years	**Same**
Classification	Class II	**Same**
Type of Test	Qualitative in vitro molecular diagnostic system	**Same**
Measurand	Detection and identification of PI*Z (rs28929474) and PI*S (rs17580) variants in the *SERPINA1* gene.	**Same** but 12 additional allelic variants in the *SERPINA1* gene (PI*I; PI*M procida; PI*M malton; PI*S iiyama; PI*Q0 granite falls; PI*Q0 west; PI*Q0 bellingham; PI*F; PI*P lowell; PI*Q0 mattawa; PI*Q0 clayton, PI*M heerlen).
Specimen Type	Genomic DNA extracted from human saliva samples	**Same**
Sample Preparation Method	DNA extraction	**Same**
Comparison with Sanger Bi-directional Sequencing	Overall agreement was 100% (P*Z:207/207; P*S: 202/202) with bi-directional sequencing.	**Same.** Overall agreement for 14 variants was 100% (227/227) with bi-directional sequencing.
Reproducibility/Precision	Reproducibility for CLIA-labs (included in DEN140044 PGS test for Bloom syndrome): two labs, 105 saliva samples (collected using the OGD-500.001), QC failure rates: First run: site 1: 1/105 (1%); site 2: 18/105 (17.1%)). First run retested: site 1: 0/105 (0%); site 2: 8/105 (7.6%)).	Reproducibility for CLIA-lab: one lab (Matrix Clinical Labs) and manufacturer, 110 saliva samples (collected using the OCD-100.014), Failure rate: site 1: 0/110 (0%); site 2: 0/110 (0%).

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Item	Predicate Device: 23andMe Personal Genome Service (PGS) for A1AT (DEN160026/DEN140044)	Candidate Device: AlphaID At Home Genetic Health Risk Service
User Comprehension Study	User Comprehension Study: 104 participants (for A1AT arm, after exclusion), 1 report (2 variants detected; not at risk), comprehension concepts (Results, Purpose, Meaning of Results, Limitations, Inheritance, Follow-up), comprehension rate per domain (89.4 – 94.2%).	User Comprehension Study: 525 participants (after exclusion), 5 reports (covering the concepts of number of variants (0, 1, 2 and variant not determined) and the 4 risk categories), at least 100 participants per report type, comprehension concepts (Results, Purpose, Limitations, Ethnicity, Other factors, Next Steps), comprehension rate per domain (94% - 99.5%).
Endogenous Interfering Substances	From 23andMe Personal Genome Service Carrier Screening Test for Bloom Syndrome (DEN140044): N = 4 endogenous agents were tested in saliva: salivary α-amylase, hemoglobin, IgA, and total protein. There was no impact on test performance with all interferents tested.	N=4 endogenous agents were tested in saliva: salivary α-amylase, hemoglobin; IgA and total protein. There was no impact on test performance with all interferents tested.
Exogenous Interfering Substances	From 23andMe Personal Genome Service Carrier Screening Test for Bloom Syndrome (DEN140044): N = 6 exogenous agents were tested in saliva samples collected after performing the following actions: eating food containing beef, eating food not containing beef, drinking alcohol, chewing gum, using mouthwash, and smoking. There was no impact on test performance at the 30 minute timepoint with all interferents tested.	N=7 exogenous agents were tested in saliva samples collected after performing the following actions: eating food without beef, eating food with beef, drinking, smoking, chewing gum, mouth washing and brushing teeth. There was no impact on test performance at the 30 minute timepoint with all interferents tested.
Microbial Interfering Substances	From 23andMe Personal Genome Service Carrier Screening Test for Bloom Syndrome (DEN140044): N = 5 microbial agents were tested in saliva: Staphylococcus epidermis, Streptococcus mutans, Lactobacillus casei, A., and Candida albicans. There was no impact on performance with all interferents tested	N=5 microbial agents were tested in saliva: Staphylococcus epidermis, Streptococcus mutans, Lactobacillus casei, Actinomyces viscosus and Candida albicans. There was no impact on performance with all interferents tested.
Clinical Studies	Clinical performance was assessed using published data.	Same
DIFFERENCES		
Sample collection device	Oragene Dx model OGD-500.001 (FDA-cleared for OTC)	ORAcollect Dx (custom version OCD-100.014) (currently in the process of getting FDA clearance for OTC, refer to K212745)

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Item	Predicate Device: 23andMe Personal Genome Service (PGS) for A1AT (DEN160026/DEN140044)	Candidate Device: AlphaID At Home Genetic Health Risk Service
Test principle	Qualitative genotyping. Multiplex assay using a customized genotyping chip (BeadChip v4 assay) and instrumentation manufactured by Illumina, for single nucleotide polymorphism detection. The raw data is generated using Illumina GenomeStudio software.	Qualitative genotyping. Polymerase chain reaction (PCR) and hybridization-based *in vitro* diagnostic test for single nucleotide polymorphism detection to be used with the Luminex 200™ instrument (with xPONENT® software) and A1AT Genotyping Test Analysis Software.
Analytical Sensitivity	The performance requirement for the PGS has been set at a minimum of 15 ng/µl DNA and maximum of 50 ng/µl DNA.	The performance requirement for the A1AT Genotyping Test has been set at a minimum of 0.0215 ng/µl DNA.
Special Instrument Requirements	The 23andMe PGS Genetic Health Risk Tests for Hereditary Thrombophilia, Alpha-1 Antitrypsin Deficiency, Alzheimer's disease, Parkinson's disease, Gaucher Disease Type I, Factor XI Deficiency, Celiac Disease, and Glucose-6-Phosphate-Dehydrogenase Deficiency, Early-Onset Primary Dystonia and Hereditary Hemochromatosis are to be performed using the Tecan Evo and Illumina iScan instruments. GenomeStudio is a modular software application that is used to view and analyze genotypic data obtained from the iScan. Coregen software conducts a variety of control checks on the file, resulting in a final genotype profile for each sample. These data are used to generate test reports on a user's genotype and associated risk of disease.	The extraction of DNA (saliva samples) and PCR reaction using A1AT Genotyping Test kit are performed with Biomek instrument. The A1AT Genotyping Test Kit used for detection and identification of 14 allelic variants and their associated alleles found in the A1AT codifying gene *SERPINA1* is to be used with the Luminex 200™ instrument (with xPONENT® software). Raw data from the Luminex System (csv. files containing the MFI value for each bead type) is processed with the A1AT Genotyping Test ANALYSIS SOFTWARE to provide allelic variant genotypes, which are subsequently converted into associated alleles, based on current scientific evidence. Additionally, the software application also provides the type of Genetic Health Risk Report associated with the identified alleles, which is subsequently used as the basis for the generation of personalized reports by the AlphaID™ At Home Genetic Health Risk Service website and result portal. Depending on the specific variant combination detected, the AlphaID™ At Home Genetic Health Risk Service provides the individuals' genetic health risk for developing lung and liver disease linked to AATD.

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Item	Predicate Device: 23andMe Personal Genome Service (PGS) for A1AT (DEN160026/DEN140044)	Candidate Device: AlphaID At Home Genetic Health Risk Service
Lung Risk Categorization (Common variants)	PI*M/PI*M: Not Likely at risk PI*M/PI*S: Not Likely at increased risk PI*M/PI*Z: Non-smokers: Not likely at increased risk/ Smokers: increased risk PI*S/PI*S: Not likely at increased risk PI*S/PI*Z: Non-smokers: Not likely at increased risk/20-50% Smokers will develop signs of emphysema during their lifetime PI*Z/PI*Z: Increased risk	PI*M/PI*M: **Same** PI*M/PI*S: **Same** PI*M/PI*Z: Non-smokers: **Same.** Smokers: Slightly at increased risk (supported by clinical cases) PI*S/PI*S: **Same** PI*S/PI*Z: Slightly at increased risk (supported by clinical cases) PI*Z/PI*Z: **Same**
Liver Risk Categorization (Common variants)	PI*M/PI*M: Not Likely at risk PI*M/PI*S: Not Likely at increased risk PI*M/PI*Z: Not likely at increased risk. PI*S/PI*S: Not likely at increased risk PI*S/PI*Z: Not likely at increased risk. PI*Z/PI*Z: Increased risk	PI*M/PI*M: **Same** PI*M/PI*S: **Same** PI*M/PI*Z: Slightly at increased risk (supported by clinical cases) PI*S/PI*S: **Same** PI*S/PI*Z: Slightly at increased risk (supported by clinical cases) PI*Z/PI*Z: Slightly at increased risk (supported by clinical cases)
Interfering Mutations	Interfering Mutations for Alph-1 Antitrypsin Deficiency: Nine potentially interfering mutations were identified for PI*Z *SERPINA1* and six potentially interfering mutation in PI*S *SERPINA1*. The potentially interfering mutations include: rs148362959, rs533419579, rs551595739, rs201774333, rs143370956, rs1131139, rs200945035, rs373630097 and rs9630 for PI*Z variant and rs538675821, rs550592374, rs141095970, rs149537225, rs1049800 and rs2230075 for PI*S variant. Interference due to these mutations was not tested.	The performance of this test may be affected by the presence of rare variants, such as rs149537225 for PI*S (rs17580); rs143370956, rs201774333, rs551595739, and rs372571769 for PI*Z (rs28929474); rs199422213 for P*I (rs28931570), PI*M procida (rs28931569), PI*M malton (rs775982338) and PI*S iiyama (rs55819880); rs544632177 and rs577164283 for PI*F (rs28929470); rs1049800 for PI*P lowell (rs121912714); rs61761869 and rs372571769 for PI*M heerlen (rs199422209); rs148207011 for PI*Q0 granite falls (rs267606950) and PI*Q0 west (rs751235320); rs200634040 and rs72552401 for PI*Q0 bellingham (rs199422211); rs148362959 and rs372571769 for PI*Q0 mattawa (rs763023697), and rs143329723, rs121912712 and rs372571769 for PI*Q0 clayton (rs764325655).

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L. TEST PRINCIPLE

The AlphaID™ At Home Genetic Health Risk Service is performed by CLIA-certified laboratory using Alpha-1 antitrypsin (A1AT) Genotyping Test (K211115). A1AT Genotyping Test utilizes Luminex xMAP technology. Genomic DNA is extracted from from human saliva samples collected as buccal swabs using ORAcollect·Dx OCD-100.014. Extracted DNA is amplified and biotinylated by multiplex PCR and PCR products are denatured and hybridized to oligonucleotide probes coupled to color-coded beads. Hybridized DNA is labeled with a fluorescent conjugate and the resulting signal is detected with a Luminex® 200 system (with xPONENT® software). Raw data obtained is processed with the A1AT Genotyping Test ANALYSIS SOFTWARE. The A1AT Genotyping Test ANALYSIS SOFTWARE algorithm converts the allelic variant genotypes into associated alleles, based on the current literature. Additionally, this software application also provides an associated template number for each sample, this is, a code that defines the type of Genetic Health Risk Report that will be generated for each individual, depending on its combination of variants or Sample Result. This template number will be subsequently used as the basis for the generation of personalized reports by the AlphaID™ System.

M. PERFORMANCE CHARACTERISTICS

The analytical and clinical studies conducted to support the intended use and substantial equivalence claim to the predicate device are summarized below.

1. Analytical Performance

a. Reproducibility/Precision

Lot-to-lot repeatability: See K211115.
External Reproducibility: See K171868.

CLIA-Certified Laboratory Verification Study:
A total of 110 samples collected with AlphaID™ At Home Saliva Collection kit in an over the counter (OTC) environment were processed with the A1AT Genotyping Test at Progenika following the Package Insert and afterwards at Matrix Clinical Clinical Labs following the internal Standard Operational Procedure (SOP) that will be used afterwards during routine testing of the AlphaID™ At Home Genetic Health Risk Service. The acceptance criteria for the study were fulfilled (concordance ≥99% and "Invalid Tests" ≤2%). The concordance between A1AT Genotyping Test results obtained in Matrix Clinical Labs and Progenika was 100% per reported variant and overall, among all tested samples. No "Invalid Tests" results were observed at Matrix

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Clinical Labs. In conclusion, this study verifies that the CLIA laboratory designated to provide the AlphaID™ At Home Genetic Health Risk Service, Matrix Clinical Labs, is able to perform the analytical procedure with A1AT Genotyping Test correctly, using human saliva samples collected with the AlphaID™ At Home Saliva Collection kit (ORAcollect®·Dx OCD-100.014) in an OTC-like setting

b. Reagent Stability

See K171868 for initial Real-Time and Open-Vial Stabilities information and study designs and K192858 for final claimed stabilities of 24 months reagent stability when stored at 2-8ºC and up to 9 months reagent stability after the vials were first opened.

c. Specimen Stability

See K152464 and K192858 for saliva samples stability collected in ORAcollect·Dx OCD-100.014 (customized version of ORAcollect·Dx OCD-100).

d. Shipping Stability

Saliva samples for testing are shipped in the AlphaID™ At Home Saliva Collection kit. See K152464 for sample shipping stability information.

e. Lower Limit of Detection (LoD)

See K211115 for Lower Limit of Detection (LoD) information.

f. DNA Extraction Variability

See K192858 for DNA Extraction Variability in saliva samples collected in ORAcollect·Dx OCD-100.014 (customized version of ORAcollect·Dx OCD-100).

g. Cross-reactivity and Cross-contamination

See K171868 for Cross-reactivity and Cross-contamination information.

h. Interfering Substances

See K192858 for Interfering Substances information in Saliva samples collected in ORAcollect·Dx model OCD-100 and equivalent ORAcollect·Dx

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OCD-100.014.

i. Interfering variants

See K192858 for information about potentially interfering variants.

2. Comparison Studies

a. Method Comparison with the Predicate

Method Comparison study in saliva samples collected in ORAcollect·Dx OCD-100.014 (customized version of ORAcollect·Dx OCD-100):

A method comparison study was performed to assess the accuracy of A1AT Genotyping Test to correctly detect the genetic variants. A total of 227 samples representing all genetic variants interrogated by the assay were analyzed and compared with Bi-Directional-Sequencing (BDS) (reference method). Percent Agreement (PA) between the two methods for the overall variants and samples (14 variants and 227 samples) was 100% (227/227) with a 95% confidence interval 98.3% to 100%. The percentage of overall "Invalid Tests" was 0% (0/227) with 95% confidence interval 0% to 1.7%.

3. Clinical Studies

a. Clinical Performance

The AlphaID™ At Home Genetic Health Risk Service has been developed for the detection of 14 variants in the *SERPINA1* gene associated with alpha1-antitrypsin deficiency (AATD), including the most common ones. Depending on the specific variant combination detected, the AlphaID™ At Home Genetic Health Risk Service provides the individuals' genetic health risk for developing lung and liver disease linked to alpha1-antitrypsin deficiency (AATD).The risk categorization is based on the reported clinical cases (published references) for each genetic result.

The AlphaID™ At Home Genetic Health Risk Service uses four (4) categories to define risk:

- **Increased risk:** There is an increased risk of developing lung or liver disease linked to AATD compared to the general population*. The chance of developing lung or liver disease linked to AATD is higher than that of the

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general population. Above 80% of people with this genetic result develop lung or liver disease during their lifetime.

- **Slightly at Increased risk:** There is a slightly increased risk of developing lung or liver disease linked to AATD compared to the general population*. The chance of developing lung or liver disease linked to AATD is slightly higher than that of the general population. 20-80% of people with this genetic result develop lung or liver disease during their lifetime.

- **Not likely at increased risk:** There is average risk of developing lung or liver disease linked to AATD compared to the general population*. The chance of developing lung or liver disease linked to AATD is similar to that of the general population. Below 20% of people with this genetic result develop lung or liver disease during their lifetime.

- **Unknown risk:** The risk of developing lung or liver disease linked to AATD is not known due to the lack of reported clinical cases or inconclusive data. The chance of developing lung or liver disease linked to AATD is unknown. More clinical studies are needed to determine the risk level.

*General population is defined as all adults who reside in the United States.

When "No Variants" are detected by the Service, the result will show "Not Likely at Risk for AATD".

b. User Comprehension Studies

AlphaID™ At Home Genetic Health Risk Service report user comprehension study:

The user comprehension study for the AlphaID™ At Home Genetic Health Risk Service showed that a demographically diverse US population of naïve users (525 participants) of the Service reports had excellent comprehension of the service's purpose, limitations, results, relevance of ethnicity, other factors that may impact test results, and appropriate next steps. Comprehension was tested through a two-step process. First, participants' comprehension was tested prior to viewing the educational module and Service reports. Second, participants were shown the educational module and the Service reports. Participants completed a survey after the first and second step. As a result, each comprehension domain achieved a minimum of 90.1% or higher user comprehension score in the first step, and 94.0% or higher user comprehension score in the second step, across all reports. The overall comprehension scores were of 92.7% and 96.8% across all comprehension domains and reports, for the first and second step respectively.

AlphaID™ At Home Saliva Collection kit user study:

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See K212745.

N. INSTRUMENT NAME

Luminex 200™ instrument with xPONENT® software.

O. SYSTEM DESCRIPTION

1. Modes of Operation:

The Luminex 200™ System is a flexible analyzer based on the principles of flow cytometry that enables you to multiplex up to 100 analytes in a single microplate well, using very small samples.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes X or No _____

Level of Concern:
Moderate

Software Description:

A1AT Genotyping Test ANALYSIS SOFTWARE: this software application is provided as part of the A1AT Genotyping Test device and it is used by the laboratory to process raw fluorescence data (csv. file) obtained from Luminex 200™ instrument with xPONENT software to obtain the genotyping results and associated health risk report template number.

AlphaID Genetic Health Risk Service Website and Results Portal (AlphaID System): this software application is a website in charge of controlling and managing the whole service, since a consumer is ordering a Saliva Collection Kit until a final report is generated based on template number and provided.

Revision Level History:
A software revision history record for the A1AT Genotyping Test ANALYSIS SOFTWARE and AlphaID™ At Home System were acceptable.

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Unresolved Anomalies:
There are no known unresolved anomalies associated with the system softwares.

EMC Testing:
Not applicable.

3. Specimen Identification

Consumers must register their saliva collection kit, linking their saliva sample to a secure online account through a unique barcode, in order to access to their results report. The unique barcode is matched to records card of kits shipped to consumers to ensure it is a valid kit. A timestamp of the consumer completing the entries to register the kit is recorded. The saliva sample is processed and result reported by the laboratory using a traceable kit barcode.

4. Specimen Sampling and Handling

Saliva samples should be collected using the AlphaID™ At Home Saliva Collection kit (ORAcollect·Dx OCD-100.014 from DNA Genotek) collection kit.
Using the provided instructions for use, the consumer uses the integrated sponge on the device to collect a saliva sample from the mouth. After saliva is collected, the cap is removed from the tube, inverted to place the sponge into the collection tube with the stabilizing liquid, and re-capped with the sponge remaining inside the tube. Upon contacting saliva cells, the stabilizing liquid lyses cellular and nuclear membranes to release and stabilize nucleic acids (DNA). Samples can be immediately processed, transported or stored for future use. Device and sample integrity are preserved during typical ambient transport and storage conditions.

5. Calibration

Calibration and verification procedures are established to demonstrate continued accuracy of the test systems.

6. Quality Control

The AlphaID™ At Home Genetic Health Risk Service uses one (1) negative control (NTC) and one (1) positive control (synthetic plasmids) included with each run. The control material is genotyped using A1AT Genotyping Test performed on Luminex 200^{TM} instrument according to routine SOPs at the laboratory.

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P. PROPOSED LABELING

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809 as applicable, and the special controls for this device type.

Q. CONCLUSION

The Intended use, technological and performance characteristics can be considered equivalent between the candidate and the predicate device. Therefore, the 23andMe Personal Genome Service (PGS) Genetic Health Risk Test for Alpha-1 Antitrypsin Deficiency is an appropriate predicate device for the AlphaID At Home Genetic Health Risk Service.

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809 as applicable, and the special controls for this device type.