May 13, 2021

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

Re: K211115
Trade/Device Name: A1AT Genotyping Test
Regulation Number: 21 CFR 866.5130
Regulation Name: Alpha-1-antitrypsin immunological test system
Regulatory Class: Class II
Product Code: PZH
Dated: April 12, 2021
Received: April 14, 2021

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 (Katelin) Mao, Ph.D.
Chief
Division of Immunology
and Hematology Devices
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)*
K211115

Device Name
A1AT Genotyping Test

Indications for Use *(Describe)*
The Progenika A1AT genotyping kit is a qualitative, polymerase chain reaction (PCR) and hybridization-based in vitro diagnostic test to be used with the Luminex 200 instrument (with xPONENT software) for the simultaneous detection and identification of 14 allelic variants and their associated alleles found in the Alpha-1 antitrypsin (A1AT) codifying gene SERPINA1. The test is intended for use with genomic DNA extracted from human whole blood samples collected as dry blood spots (DBS) or in K2-EDTA or from human saliva samples collected as buccal swabs using ORAcollect·Dx OCD-100. The A1AT allelic variant genotypes and associated allele results, when used in conjunction with clinical findings and other laboratory tests, are intended as an aid in the diagnosis of individuals with A1AT deficiency (A1ATD). The kit is indicated for prescription use only.

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.

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Special 510(k) Summary

A. Name of the device: A1AT Genotyping Test

B. Common name: Test for SERPINA1 gene genotyping

C. Regulatory information:

a. Classification: Class II

b. Regulation Section: 21 CFR 866.5130, Alpha-1-antitrypsin immunological test system

c. Classification Product Code: PZH, *SERPINA1* Variant Detection System

d. Review panel: Immunology (82)

D. Applicant: Progenika Biopharma S.A.

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Contact person: Diego Tejedor, Technical Director
e-mail: diego.tejedor@grifols.com

E. Intended Use:

The Progenika A1AT genotyping kit is a qualitative, polymerase chain reaction (PCR) and hybridization-based in vitro diagnostic test to be used with the Luminex 200TM instrument (with xPONENT® software) for the simultaneous detection and identification of 14 allelic variants and their associated alleles found in the Alpha-1 antitrypsin (A1AT) codifying gene SERPINA1. The test is intended for use with genomic DNA extracted from human whole blood samples collected as dry blood spots (DBS) or in K2-EDTA or from human saliva samples collected as buccal swabs using ORAcollect·Dx OCD-100. The A1AT allelic variant

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genotypes and associated allele results, when used in conjunction with clinical findings and other laboratory tests, are intended as an aid in the diagnosis of individuals with A1AT deficiency (A1ATD).

The kit is indicated for prescription use only.

F. Device Description:

Alpha 1 antitrypsin (A1AT) Genotyping Test utilizes Luminex xMAP technology. Genomic DNA is extracted from DBS, from human EDTA anticoagulated whole blood or from human saliva samples collected as buccal swabs using ORAcollect·Dx OCD-100. 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. Raw data obtained is processed with the A1AT Genotyping Test ANALYSIS SOFTWARE in order to obtain the final report. The A1AT Genotyping Test ANALYSIS SOFTWARE algorithm converts the allelic variant genotypes into associated alleles, based on the current literature.

The A1AT Genotyping Test Kit is composed of 4 reagent components (A1AT PCR Master Mix, A1AT Beads Master Mix, SAPE, SAPE Dilution Buffer) required to perform all the abovementioned processing steps. The A1AT Genotyping Test ANALYSIS SOFTWARE, instructions for use and other necessary files are uploaded on a Grifols website. Two kit configurations are available: for 48 or 192 tests (different amounts of the same reagent components are provided in each case).

G. Substantial Equivalence Information:

Predicate Device: A1AT Genotyping Test

510(k) number: K192858

Applicant: Progenika Biopharma S.A.

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Main conclusion: The similarities among the candidate device and the predicate device show that A1AT Genotyping Test to be used together with the updated software application is substantially equivalent to the predicate.

Based on the risk assessment and performance data, it can be considered that the differences due to the software update do not raise different questions of safety and effectiveness.

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Comparison table:

Item	Candidate Device Modified A1AT Genotyping Test	Predicate Device A1AT Genotyping Test (K192858)
Intended Use	The Progenika A1AT genotyping kit is a qualitative, polymerase chain reaction (PCR) and hybridization-based *in vitro* diagnostic test to be used with the Luminex 200™ instrument (with xPONENT® software) for the simultaneous detection and identification of 14 allelic variants and their associated alleles found in the Alpha-1 antitrypsin (A1AT) codifying gene *SERPINA1*. The test is intended for use with genomic DNA extracted from human whole blood samples collected as dry blood spots (DBS) or in K_2-EDTA or from human saliva samples collected as buccal swabs using ORAcollect·Dx OCD-100. The A1AT allelic variant genotypes and associated allele results, when used in conjunction with clinical findings and other laboratory tests, are intended as an aid in the diagnosis of individuals with A1AT deficiency (A1ATD). The kit is indicated for prescription use only	The Progenika A1AT genotyping kit is a qualitative, polymerase chain reaction (PCR) and hybridization-based *in vitro* diagnostic test to be used with the Luminex 200™ instrument (with xPONENT® software) for the simultaneous detection and identification of 14 allelic variants and their associated alleles found in the Alpha-1 antitrypsin (A1AT) codifying gene *SERPINA1*. The test is intended for use with genomic DNA extracted from human whole blood samples collected as dry blood spots (DBS) or in K_2-EDTA or from human saliva samples collected as buccal swabs using ORAcollect·Dx model OCD-100. The A1AT allelic variant genotypes and associated allele results, when used in conjunction with clinical findings and other laboratory tests, are intended as an aid in the diagnosis of individuals with A1AT deficiency (A1ATD). The kit is indicated for prescription use only
Specimen Type	**Same**	Genomic DNA extracted from human whole blood samples collected as DBS or in K2-EDTA and human saliva samples collected as buccal swabs using ORAcollect·Dx model OCD-100.
Target	**Same**	Qualitative identification of A1AT alleles (which represent the phenotypes) causing A1ATD.

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Item	Candidate Device Modified A1AT Genotyping Test	Predicate Device A1AT Genotyping Test (K192858)
Device components	Same components, except for the CD component. A1AT Genotyping Test ANALYSIS SOFTWARE and instructions for use are uploaded on a website.	The test is composed of four reagent components (A1AT PCR Master Mix, A1AT Beads Master Mix, SAPE and SAPE Dilution Buffer) in sufficient quantity for either 48 or 192 tests and a CD containing the A1AT Genotyping Test ANALYSIS SOFTWARE.
Technology	**Same**	Polymerase chain reaction (PCR) and hybridization-based *in vitro* diagnostic test to be used with the Luminex 200™ instrument (with xPONENT® software). DNA is extracted, 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 resulting signal is detected with a Luminex® 200 system. The raw data obtained is finally processed with the A1AT Genotyping Test ANALYSIS SOFTWARE in order to obtain the final report.
Software application	The software version has been updated (v1.0.8.16). Results of every study have been re-analyzed with this updated software version to ensure acceptance criteria are met.	A1AT Genotyping Test ANALYSIS SOFTWARE v1.0.6.1

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Item	Candidate Device Modified A1AT Genotyping Test	Predicate Device A1AT Genotyping Test (K192858)
Product Stability	**Same**	– Real time stability: 24 months at 2-8ºC – Open vial stability: 9 months at 2-8ºC
Performance specifications	– Lower Limit of Detection: 0.0215 ng/µl DNA. – Interferences: **Same** – Precision: o Lot-to-Lot: 100% correct calls o External reproducibility: **Same** – Accuracy: **Same**	– Lower Limit of Detection: 0.0310 ng/µl DNA. – Interferences: o For blood samples: hemoglobin, bilirubin, triglycerides and short blood draw. o For saliva samples: α-amylase, hemoglobin, immunoglobin A, total protein, microbes, eating food without beef, eating food with beef, drinking, smoking, chewing gum, mouth washing and brushing teeth. – Precision: o Lot-to-Lot: overall correct call rate of 99.7% (one M/S sample provided an incorrect result). o External reproducibility: 100% correct calls. – Accuracy: 147 samples, comparator: Bi-directional Sanger sequencing.
Intended population	**Same**	Prescription use only
DNA extraction method	Whole blood samples collected in K_2-EDTA**: same**	Whole blood samples collected in K_2-EDTA: QIAamp DNA Blood Mini Kit (Qiagen) Whole blood samples collected as DBS:

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Item	Candidate Device Modified A1AT Genotyping Test	Predicate Device A1AT Genotyping Test (K192858)
	Whole blood samples collected as DBS: **same**, although the home-made buffer will be removed. Saliva samples: **same**	– Commercial lysis and neutralization solutions (Sigma) – Home-made buffer Saliva samples: – QIAamp DNA Blood Mini Kit (Qiagen) – Commercial lysis and neutralization solutions (Sigma) – QIAsymphony DNA Mini Kit (Qiagen)
Specimen Stability	**Same**	– Whole blood samples collected in K2-EDTA: up to 24 days before DNA extraction at 2-8ºC. – Whole blood samples collected as DBS: up to 6 months at ambient temperature. Saliva samples collected as buccal swabs using ORAcollect·Dx model OCD-100 (DNA Genotek): up to 60 days when stored at ambient temperature.

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H. Performance Data:

Analytical Data:

a) Precision/Reproducibility:

Lot-to-lot repeatability: The lot-to-lot repeatability was determined by testing the "Sample Panel" (five DNA samples covering Z/Z, M/Z, S/S, M/S, and S/Z Sample Results) in triplicate with three different reagent lots, by two operators, on six non-consecutive days, alternating between two Luminex instruments. An overall repeatability of 100% was obtained for Sample Results.

External Reproducibility: See K171868.

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 K171868 for whole blood samples collected as DBS or in K2-EDTA stabilities.

See K152464 and K192858 for saliva samples stability collected in ORAcollect·Dx OCD-100.

d) Lower Limit of Detection (LoD):

The DNA concentration at which 95% of sample replicates resulted in correct Sample Results was determined by testing 20 replicates of nine DNA dilutions of the "Sample Panel" (from 0.16 to 0.0033 ng/μl) using two reagent lots. It was shown that the highest LoD among the two lots used was 0.0215 ng/μl.

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e) DNA Extraction Variability:

See K171868 for DNA Extraction Variability in whole blood samples collected as DBS or in K2-EDTA information.

See K192858 for DNA Extraction Variability in saliva samples.

f) Cross-reactivity and Cross-contamination:

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

g) Interfering Substances:

See K171868 for Interfering Substances information in whole blood samples collected as DBS or in K2-EDTA.

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

See K192858 for information about potentially interfering variants.

Comparison Data:

h) Method Comparison:

See K171868 for Method Comparison information in whole blood samples.

See K192858 for Method Comparison information in saliva samples.

I. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR 809.10.

J. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.

K. Date of summary preparation:

April 29, 2021