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510(k) Summary

A. Name of the device: ID CORE CONTROL

B. Common name: Quality Control Material

C. Classification name: Class II

D. Applicant: Progenika Biopharma S.A.

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E. Intended Use:

The ID CORE CONTROL kit contains two separate vials: ID CORE CONTROL 1 and ID CORE CONTROL 2, both composed of synthetic plasmid pools to be used as assayed positive controls for alternate alleles (alleles 1 and 2) of the 29 polymorphisms interrogated by ID CORE XT. Both control vials must be used in every run of the ID CORE XT test.

ID CORE CONTROL samples are not intended to monitor the DNA extraction step of the ID CORE XT processing protocol.

F. Device Description:

The ID CORE CONTROL kit contains two vials: ID CORE CONTROL 1 and ID CORE CONTROL 2. One replicate of each vial is required to be included in every run of the ID CORE XT test to determine run validity.

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Each ID CORE CONTROL vial (ID CORE CONTROL 1 and ID CORE CONTROL 2) contains a pool of 3 recombinant synthetic DNA plasmids resuspended in a preservative buffer. The plasmid inserts consist of chemically synthesized ID CORE XT amplicons, organized (b) (4) . Those amplicons contain the target sequences for ID CORE XT primers and the complementary sequences for ID CORE XT probes.

The expected polymorphism genotype results for ID CORE CONTROL 1 and ID CORE CONTROL 2 are shown in the table below. The PCR input volume for each sample is 5 µl, which is equal to the input volume of genomic DNA samples.

Blood Group System	Polymorphim	Polymorphism Genotype Results	
		ID CORE CONTROL 1	ID CORE CONTROL 2
Rh	*RHCE*:c.122A>G	GG	AA
	RHCE:c.307T>C	C	T
	RHCE:c.335+3039ins109	Present	Absent
	RHCE:c.676G>C	CC	GG
	RHCE:c.712A>G	GG	AA
	RHCE:c.733C>G	GG	CC
	RHCE:c.1006G>T	TT	GG
	RHD-CE-D hybrid	Present	Absent
Kell	*KEL*:c.578T>C	CC	TT
	KEL:c.841T>C	CC	TT
	KEL:c.1790C>T	TT	CC
Kidd	*SLC14A1*:c.342-1G>A	AA	GG
	SLC14A1:c.838G>A	AA	GG
	SLC14A1:c.871T>C	CC	TT
Duffy	*FY*:c.1-67T>C	CC	TT
	FY:c.125G>A	AA	GG
	FY:c.265C>T	TT	CC
MNS	*GYPA*:c.[59C>T]	TT	CC
	GYPB:c.143T>C	CC	TT
	GYPB:c.230C>T	TT	CC
	GYPB:c.270+5G>T	TT	GG
	GYP. hybrid	Present	Absent
Diego	*DI*:c.2561T>C	CC	TT
Dombrock	*DO*:c.793A>G	GG	AA
	DO:c.323G>T	TT	GG

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Blood Group System	Polymorphim	Polymorphism Genotype Results	
		ID CORE CONTROL 1	ID CORE CONTROL 2
	DO:c.350C>T	TT	CC
Colton	*CO*:c.134C>T	TT	CC
Cartwright	*YT*:c.1057C>A	AA	CC
Lutheran	*LU*:c.230A>G	AA	GG

The ID CORE XT test is a qualitative test that uses ratios of fluorescence signal intensities provided by allele specific probes to assign polymorphism genotype results. The ID CORE XT Analysis Software automatically analyses the concordance of polymorphism genotypes results obtained for ID CORE CONTROL 1 and ID CORE CONTROL 2, without requiring interpretation of the user. As such, for an ID CORE XT assay run to be considered valid, the ID CORE CONTROL samples must show 100% correct calls for the expected polymorphism genotypes. If any of the positive control samples fails during a run, an “Invalid run” message will appear and no test sample results will be provided.

G. Substantial Equivalence Information:

Predicate Device: BeadCheck HEA Positive Control

510(k) number: BK130050

Applicant: BioArray Solutions, Ltd

Main conclusion: Both devices, predicate and subject, are intended to be used as assayed positive controls to monitor the correct performance of tests for the molecular characterization of Human Erythrocyte Antigens (HEA) based on genotyping techniques. The design characteristics of both devices are also highly similar and can be considered substantially equivalent. Although some minor design differences exist, those do not raise any different questions of safety or effectiveness about the product. Therefore, the BeadCheck HEA Positive Control is an appropriate predicate device for the ID CORE CONTROL.

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Comparison table:

Item	Predicate Device: BeadCheck HEA Positive Control	Subject Device: ID CORE CONTROL	Similarity/Difference
Intended Use	The BeadCheck HEA Positive Control consists of AA and BB synthetic plasmid pools which are intended for use as assayed positive controls for the Precise Type HEA Molecular BeadChip Test. The Positive Controls are designed to demonstrate the Precise Type HEA Molecular will detect all A and B forms of each genetic marker listed. The Precise Type HEA BeadCheck kit is not intended to monitor the DNA extraction step of the Precise Type HEA Molecular Beadchip Test.	The ID CORE CONTROL kit contains two separate vials: ID CORE CONTROL 1 and ID CORE CONTROL 2, both composed of synthetic plasmid pools to be used as assayed positive controls for alternate alleles (alleles 1 and 2) of the 29 polymorphisms interrogated by ID CORE XT. Both control vials must be used in every run of the ID CORE XT test. ID CORE CONTROL samples are not intended to monitor the DNA extraction step of the ID CORE XT processing protocol.	Similarity: assayed positive controls for HEA determinations tests. Recombinant synthetic plasmids designed as homozygous genotypes of each interrogated genetic marker. They do not monitor the DNA extraction step. Difference: Specific polymorphisms genotypes interrogated.
Matrix	Preservative buffer: 10mM Tris-HCl buffer at pH8.0 with 0.09% sodium azide.	Preservative buffer: (b) (4) .	Similarity: (b) (4) Difference: (b) (4) added in ID CORE CONTROL.
Genetic Material	Each vial contains a pool of 22 unique plasmids, corresponding to the number of amplicons in the HEA BeadChip assay, inserts from PCR amplicons from human genomic DNA.	Each vial contains a pool of three different plasmids which include the sequences of different amplicons (b) (4) , inserts chemically synthesized.	Similarity: Recombinant DNA plasmid pools Difference: plasmids origin and amplicon distribution.

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Item	Predicate Device: BeadCheck HEA Positive Control	Subject Device: ID CORE CONTROL	Similarity/Difference
Physical Format	Liquid and ready to use. Input volume equal to the volume used for genomic DNA samples (for 12 uses).	Liquid and ready to use. Input volume equal to the volume used for genomic DNA samples (for 25 uses).	Similarity: liquid and ready to use. Same volume as genomic samples. Difference: maximum number of uses
Result Generation	Genotype values are generated based on the ratio of signal intensities. Genotype values and predicted phenotype results are reported. For those combinations not previously described in the literature a PV (Possible Variant) result is provided. If expected genotype and phenotype results do not exactly match the expected, the run is invalid and no results are provided for test samples. This process is carried out by a software application without user intervention.	Polymorphism genotype results are provided for ID CORE CONTROL samples based on ratios of signal intensities. When those results do not show a 100% concordance with the expected values, an "Invalid Run" message will be obtained and no result for test samples included in the run will be provided. ID CORE XT Analysis Software automatically confirms run validity before providing results for test samples.	Similarity: use of ratios of signal intensities to assign genotype values. Software application for result interpretation. No samples results for invalid runs. Difference: no predicted phenotype results provided for ID CORE CONTROL.
Storage	Storage temperature -20ºC. Shelf-life and open-vial stability up to 12 months.	Storage temperature 2-8ºC. Shelf-life of at least 15 months and open-vial stability up to 12 months at 2-8ºC.	Similarity: at least 12 months stability. Difference: storage temperature and maximum shelf-life.

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H. Performance Data:

Analytical Data:

a) Matrix Effects:

A matrix effect study was performed in order to compare the results obtained with ID CORE XT for the ID CORE CONTROL matrix and different genomic DNA sample matrices as material inputs.

The samples tested by ID CORE XT are genomic DNAs extracted from whole blood using different DNA extraction kits. Hence elution buffers used for DNA extraction and/or DNA storage and preservation (Qiagen AE and ATE buffers, PureLink Genomic Elution Buffer and TE buffer) were tested in with ID CORE XT, in parallel with ID CORE CONTROL matrix. The ID CORE XT results for the matrix material was expected to be equivalent to that of the tested elution buffers, as well as to a Negative Control sample, since none of them contain human DNA templates.

Every tested buffer, as well as the ID CORE CONTROL matrix provided results which were consistent with a valid Negative Control sample. Therefore, it was concluded that there is no matrix effect on ID CORE CONTROL.

b) Repeatability and Reproducibility Study:

A repeatability and reproducibility study was conducted in order to evaluate the repeatability and reproducibility of ID CORE CONTROL across lots (3), operators (3), and days (3).

Three operators performed three independent runs (one run per ID CORE CONTROL lot), during three non-consecutive days. Each operator tested ten (10) replicates of each ID CORE CONTROL sample (ID CORE CONTROL 1 and ID CORE CONTROL 2) with three (3) different ID CORE CONTROL lots each testing day. A total of 270 ID CORE CONTROL 1 and 270 ID CORE CONTROL 2 (3 operators x 3 lots x 3 days x 10 replicates) were analyzed throughout the study. All the lots, days and operators provided a Valid run, indicating that the polymorphism genotype results of all the ID CORE CONTROL samples were 100% concordant with those expected.

In conclusion, this study showed that ID CORE CONTROL demonstrates acceptable repeatability and reproducibility across operators (100%), reagent lots (100%), and testing days (100%).

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c) Lot-to-lot Verification Study:

A Lot-to-Lot Verification study was performed to verify the consistency of the ID CORE CONTROL polymorphism genotype results when combining different lots of ID CORE CONTROL and ID CORE XT.

Three (3) different lots of ID CORE CONTROL were tested with three (3) different lots of ID CORE XT, for a total of nine (9) combinations. Each ID CORE XT lot was used in combination with a different lot of DNA Polymerase enzyme. For each product combination, ten (10) replicates of each ID CORE CONTROL samples (ID CORE CONTROL 1 and ID CORE CONTROL 2) were evaluated. A total of 90 ID CORE CONTROL 1 and 90 ID CORE CONTROL 2 samples were analyzed (10 replicates x 3 ID CORE XT lots x 3 ID CORE CONTROL lots samples). All the runs performed provided a Valid run, indicating that the polymorphism genotype results of ID CORE CONTROL samples were 100% concordant with those expected.

The study showed that the ID CORE CONTROL demonstrates acceptable lot-to-lot variation when tested with different ID CORE XT and DNA polymerase lots.

d) Guard Banding Studies:

ID CORE CONTROL samples consist of DNA plasmid pools for use as assayed positive controls during the testing of genomic samples with ID CORE XT. Due to the fact that DNA plasmids are intrinsically different from genomic DNA samples, Guard Banding and Surrogate studies were conducted to verify that ID CORE CONTROL samples are as sensitive as genomic DNA samples to protocol variations at key steps of the ID CORE XT assay procedure.

The range of values for each assay parameter yielding acceptable test results for both, ID CORE CONTROL and genomic DNA samples, is presented in the table below. The results demonstrated that for 16 out of the 17 test cases, the acceptable range for ID CORE CONTROL is identical or narrower than for a genomic DNA sample.

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ID CORE XT processing step	Test case group definition	Nominal value	Acceptable range	
			ID CORE CONTROL	Genomic DNA samples
Amplification, Hybridization, Labeling	Mixing of reagents by vortexing and spin down reagents by pulse centrifugation	3-5 sec	1-10 sec	1-10 sec
Amplification	PCR master mix volume and PCR reaction mix volume	20 µl	5 µl-80 µl	5 µl-80 µl
	Enzyme (Taq) volume in PCR reaction mix	0.5 µl	0.1µl-2 µl	0.1µl-2 µl
	Time for dispensation of PCR reaction mix and addition of DNA samples	Immediate-up to 60 min	Immediate-120 min	Immediate-120 min
	PCR product stability	2-8ºC: up to 72 h	Immediate-96 h	Immediate-96 h
		-20ºC: up to 4 weeks	Up to 5 weeks	Up to 5 weeks
Hybridization	Mixing time of Beads Master Mix	10-15 sec	5 sec-30 sec	5 sec-30 sec
	Beads Master Mix Volume	46 µL	14-92 µL	24-92 µL
	Time for dispensation of Beads Master Mix and addition of PCR product	Immediate-up to 30 min	Immediate-60 min	Immediate-60 min
	Volume of PCR product in hybridization step	4 µL	1-7 µL	1-8 µL
Labeling	Volume of SAPE in the labeling mix	4 µL	3-5 µl	2-5 µl
	Time for labeling mix storage	Up to 35 min	Immediate-70 min	Immediate-70 min
	Time for labeling mix dispense	Immediate-up to 5 min	Immediate-10 min	Immediate-10 min
	Labeling time	10 min	5 min-20 min	5 min-20 min
Data Acquisition	Transfer time from labeling to Luminex instrument	Immediate-up to 10 min	Immediate-20 min	Immediate-20 min
	Temperature of data acquisition on Luminex	52ºC	47ºC-57ºC	47ºC-57ºC
	Reading time using Luminex instrument	Time required for reading 4-96 tests	Immediate-45 min	Immediate-45 min

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ID CORE CONTROL has a wider acceptable range than genomic DNA samples when low volumes of Beads Master Mix are used. As such, ID CORE CONTROL samples may not indicate procedural errors when half the recommended volume or less of ID CORE XT Beads Master Mix is pipetted.

In addition, since ID CORE CONTROL can be less sensitive to changes in Veriti Dx thermal cycler settings for ID CORE XT Amplification and Hybridization steps, the use of the correct program settings should be verified in each thermal cycler run.

e) Stability Studies:

Real-time Stability: A Real Time Stability Study was performed to determine the self-life stability of the ID CORE CONTROL when stored at 2-8ºC.

Three different ID CORE CONTROL lots were stored at 2-8ºC and tested at time points 3, 6, 9, 10, 12, 13, 15 and 16 months after manufacturing. At every time point, the polymorphism genotype calls for all ID CORE CONTROL samples and replicates were 100% coincident with those expected.

This data demonstrated that ID CORE CONTROL kits are stable for at least 15 months after manufacturing when stored at 2-8ºC.

Open Vial Stability: An Open Vial Stability Study was performed to evaluate the in-use stability of ID CORE CONTROL after having been put into use and stored at 2-8ºC. The in-use stability testing is designed to simulate the maximum 25 time uses of the ID CORE CONTROL samples (designed for 25 uses).

After 3 months of storage at 2-8ºC, ID CORE CONTROL vials were first opened and tested on that time point (T3), and at months 5, 7, 10, 12 and 15 after manufacturing, corresponding to 5, 10, 15, 20, and 25 in-use cycles, respectively. A Valid run was obtained at every time point for every tested sample.

In conclusion, ID CORE CONTROL kits have proved stability up to 12 months for 25 uses after the vials were first opened, for kits that had been previously stored for 3 months at 2-8ºC after manufacturing and before being opened for the first time.

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Stress Stability: A Stress Stability Study was performed with the aim of evaluating the impact of extreme temperature excursions that may be encountered during global transport delivery on ID CORE CONTROL stability.

Nine months old kits were subjected to either, high temperature (25ºC) stress cycles, or freeze/thaw cycles, and tested on that time point (T9), and at months 12, 13, 15 and 16 after manufacturing. A “Valid run” message was obtained at every time point for every tested sample.

In conclusion, the obtained data demonstrate that ID CORE CONTROL kits stored at 2-8ºC for 9 months are stable up to 6 additional months at 2-8ºC after having been exposed to the stress conditions of a total of 8 days at 25ºC or 6 freeze/thaw cycles.

I. Proposed Labeling:

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

J. Conclusion:

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

K. Date of summary preparation:

August 4, 2017.