March 21, 2023

Genomadix Inc.
Amanda Dwyer
Quality & Regulatory
340 Legget Drive, Suite 180
Kanata (Ottawa), Ontario
Canada

Re: K220026
Trade/Device Name: Genomadix Cube CYP2C19 System
Regulation Number: 21 CFR 862.3360
Regulation Name: Drug Metabolizing Enzyme Genotyping System
Regulatory Class: Class II
Product Code: NTI
Dated: November 1, 2022
Received: November 1, 2022

Dear Amanda Dwyer:

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,

Paula Caposino -S

Digitally signed by Paula Caposino -S
Date: 2023.03.21 11:25:36 -04'00'

Paula Caposino, Ph.D.
Acting Deputy Director
Division of Chemistry
and Toxicology 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)*
k220026

Device Name
Genomadix Cube CYP2C19 System

Indications for Use *(Describe)*
The Genomadix Cube CYP2C19 System is a qualitative in vitro diagnostic test for the identification of a patient's CYP2C19 *2, *3, and *17 genotypes determined from genomic DNA obtained from a buccal swab sample.

The Genomadix Cube CYP2C19 System can be used to aid clinicians in determining therapeutic strategy for therapeutics that are metabolized by the cytochrome P450 2C19 gene product, specifically *2, *3, and *17 alleles. This test is not intended to be used to predict drug response or non-response.

The Genomadix Cube CYP2C19 Test Kit is indicated for use with the Genomadix Cube CYP2C19 Platform.

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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1 510(k) Summary

510(k) Number	K220026
This 510(k) Summary is in conformance with 21CFR 807.92	

1.1 SUBMITTER

Genomadix Inc.
340 Legget Drive
Suite 180
Kanata, Ontario, Canada

Contact: Amanda Dwyer

Email: amanda.dwyer@genomadix.com

1.2 DEVICE NAME AND CLASSIFICATION

Trade Name:	Genomadix Cube CYP2C19 System
Common Name:	Cube CYP2C19 System
Classification:	Class II
CFR Reference:	21 CFR §862.3360 Drug Metabolizing Enzyme Genotyping Systems
Classification Panel:	Toxicology (91)
Product Code	NTI - Drug Metabolizing Enzyme Genotyping Systems

1.3 PREDICATE DEVICE

Predicate Device:	Spartan RX CYP2C19 Test System, k123891

1.4 INDICATIONS FOR USE:

The Genomadix Cube CYP2C19 System is a qualitative in vitro diagnostic test for the identification of a patient's CYP2C19 *2, *3, and *17 genotypes determined from genomic DNA obtained from a buccal swab sample.

The Genomadix Cube CYP2C19 System can be used to aid clinicians in determining therapeutic strategy for therapeutics that are metabolized by the cytochrome P450 2C19 gene product, specifically *2, *3, and *17 alleles. This test is not intended to be used to predict drug response or non-response.

The Genomadix Cube CYP2C19 Test Kit is indicated for use with the Genomadix Cube CYP2C19 Platform.

1.5 PLATFORM, DEVICE DESCRIPTION & TEST PRINCIPLE

The Genomadix Cube CYP2C19 System is a sample-to-result DNA testing system that uses proprietary technology to integrate DNA extraction and amplification. Genotypes are determined using Polymerase Chain Reaction (PCR) and fluorescent probe detection.

The test protocol is based on the following major processes:

a. Collection of human genomic DNA via swab(s)
b. DNA extraction
c. PCR amplification of extracted DNA

d. Detection of amplified PCR products via fluorescent oligonucleotide probes
e. Fluorescent signal detection and analysis (determination of CYP2C19 *2, *3, and *17 genotypes)

NOTE: Steps (b) through (e) are automated by the CYP2C19 System.

Results are presented to the user as a genotype call. External Controls and internal software-based controls monitor performance and automatically inform the user of anomalies in the instrument and reagents.

The Genomadix Cube CYP2C19 System has two internal controls that run automatically during each test, Internal Positive Control which displays an “Inconclusive”, and a Positive System Control (PSC) which displays a “PSC”. If an INCONCLUSIVE or PSC result is displayed, restart at Step 1 of the workflow, collect a new set of swabs from the same patient to test using a new cartridge.

1.6 SUBSTANTIAL EQUIVALENCE TECHNOLOGICAL COMPARISON

Similarities		
Item	**Subject Device: Genomadix Cube CYP2C19 System**	**Predicate Device: Spartan RX CYP2C19 Test System (K123891)**
Intended Use	The system is a qualitative in vitro diagnostic test for the identification of a patient’s CYP2C19 *2, *3, and *17 genotypes determined from genomic DNA obtained from a buccal swab sample.	Same
Indications for use	The Genomadix Cube CYP2C19 System can be used to aid clinicians in determining therapeutic strategy for therapeutics that are metabolized by the cytochrome P450 2C19 gene product, specifically *2, *3, and *17 alleles. This test is not intended to be used to predict drug response or non-response. The Genomadix Cube CYP2C19 System is not indicated for stand-alone diagnostic purposes. The information provided from this test may supplement decision making and should only be used in conjunction with routine monitoring by a physician. Clinicians should use professional judgment in the interpretation of results from this test. Results from this type of assay should not be used in predicting a patient’s response to drugs for which the drug metabolizing enzyme activity of that allele, or the drug metabolic pathway, has not been clearly established.	Same
Prescription/ Over the Counter	For prescription use only.	Same
Limitation	Not intended to be used to predict drug response or non-response.	Same
DNA Sequence	Detects specific DNA sequences through recognition of DNA targets	Same
Technology	Utilizes thermal cycling and target DNA amplification; fluorescent probe detection	Same
Assay Results	Assay signal results are interpreted by a software program. Assay results are provided as genotype calls reported to the end user in a report format.	Same
Target Gene, Mutation	CYP4502C19 *2, *3 and *17.	Same
Specimen Type	DNA from a buccal swab sample.	Same
Platform	Fluorescent probe PCR-based genotyping test for multiplex analysis of DNA sequences.	Same

Differences		
Item	**Subject Device: Genomadix Cube CYP2C19 System**	**Predicate Device: Spartan RX CYP2C19 Test System (K123891)**
Swab and reagent tube configuration	A cartridge of three reagent tubes stored separately from the pouch containing the three swabs.	Each reagent tube is pouched with one swab.
Sample insertion	Buccal sample is inserted into the test cartridge at the location of testing.	Buccal sample is inserted into the reagent tube immediately after collection.
Sample transport	Buccal samples are transported at room temperature and can be analyzed within 20 hours; reagents do NOT accompany swabs; at test set-up, reagents have a bench working time of 15 minutes.	Buccal samples in reagent cartridges are transported at 2-8°C; if using the transport container, reagents are stable for 45 minutes before swabbing and 60 minutes after swabbing.

1.7 PERFORMANCE CHARACTERISTICS

1.7.1 Carryover

A total of 122 samples, were run. A quantity of sixty-one, *1/*1 genotypes tested alternately with non-*1/*1 genotypes (twenty-one *2/*17, twenty *2/*2 and twenty *17/*17) on the same set of Cubes (devices). The results generated were 99% concordant results (121/122), one inconclusive result.

Carryover First Pass					
Genotype	**# Tests**	**# Inconclusive**	**# Incorrect Calls**	**# Correct Calls**	**Correct Call Rate (%)**
*1/*1	61	2	0	59	96.7
*2/*17	21	0	0	20	100
*2/*2	20	0	0	20	100
*17/*17	20	0	0	120	100
TOTAL	**122**	**2**	**0**	**120**	**98**

Carryover Second Pass tests				
Genotype	**# Tests**	**# Inconclusive**	**# Incorrect Calls**	**# Correct Calls**
*1/*1	1	0	0	1

NOTE: The second inconclusive (no call result) was not identified during the initial test, and the second pass, result was not available. This result will be presented in the final results.

Carryover Final (Combined First and Second pass)						
Genotype	**# Tests**	**# Correct Calls**	**# Incorrect Calls**	**# Inconclusive Calls**	**Second Pass Correct Call Rate (%)**	**2-sided 95% CI Lower Limit**
*1/*1	61	60	0	1	98	91
*2/*17	21	21	0	0	100	85
*2/*2	20	20	0	0	100	84
*17/*17	20	20	0	0	100	84
TOTAL	**122**	**121**	**0**	**1**	**99%**	**96%**

1.7.2 End User Performance Summary

Based on end user studies, a second pass test is required, when the first pass gives an Inconclusive result, to achieve a point error estimate (% agreement) of 99% or better, and a 95% One-sided Confidence Lower Limit of 95% or better.

Inconclusive (INC) and Positive System Control (PSC) results are system generated internal quality controls that run automatically during each test. Refer to the Quality Control section of this document for more details on the internal controls and the CYP2C19 Operator's Manual, for information on Troubleshooting.

First Pass Performance

End User Study	Samples Tested	# INC/PSC	Incorrect Calls	Correct Call	% Agreement	95% Two-sided Confidence Lower Limit	95% One-sided Confidence Lower Limit
Inter-laboratory Reproducibility	960	9	0	951	99%	98%	98%
Method Comparison	433	17	2	414	96%	93%	94%

Final (Second Pass) Performance

New swabs collected only for those subjects for whom an inconclusive result was obtained on first pass; for a second pass (repeat) testing. Of the 25 inconclusive results shown in the table above, twenty-two (22) second pass tests were conducted. Of those, twenty (20) were resolved and the correct call was obtained. Three subjects were not available to sample for a repeat test; therefore, the inconclusive result was applied to the final result.

End User Study	Samples Tested	# INC/PSC	Incorrect Calls	Correct Call	% Agreement	95% Two-sided Confidence Lower Limit	95% One-sided Confidence Lower Limit
Inter-laboratory Reproducibility	960	3[a]	0	957	100%	99%	99%
Method Comparison	433	2	2	429	99%	98%	98%

[a] The subjects were not available to be re-run after a first pass inconclusive result was obtained; therefore, the inconclusive was applied to the final result.

1.7.3 Inter-laboratory Reproducibility

The performance of the Genomadix Cube CYP2C19 System was evaluated at three clinical sites over five non-consecutive days per site, with a total of six operators (two per site). The following table outlines the operators involved in the study, who all completed the system training and did not have extensive experience with buccal swab collection.

The results were generated from two swabbing sessions, each subject was tested by Operator 1 and Operator 2, at each site. If the result of the first pass for a particular individual was an inconclusive result, the test was repeated (second pass). The second pass test is considered the final result and has been used when calculating the performance characteristics.

On the first pass, nine samples produced inconclusive results (Lot A (3), Lot B (5), Lot C (1)). New swabs were collected only for those subjects for whom an inconclusive result was obtained. A second pass test was performed on six of the nine samples, all six samples were resolved. Three samples were not available for a second pass test; first pass inconclusive result was applied to the final result.

The overall call rate after the second pass of the Genomadix Cube CYP2C19 System is 99.7%, with a 95% two-sided lower confidence limit of 99.1%.

Inter-Laboratory Reproducibility First Pass					
Sample Type [a]	**# Samples Tested**	**# Inconclusive Calls**	**# Incorrect Calls**	**# Correct Calls [b]**	**Correct call rate (%)**
*1/*1	120	0	0	120	100
*1/*2	120	0	0	120	100
*1/*3	120	1	0	119	99
*1/*17	120	0	0	120	100
*2/*2	120	1	0	119	99
*2/*3	120	1	0	119	99
*2/*17	120	5	0	115	96
*17/*17	120	1	0	119	99
Total Samples (all sites, all lots)	**960**	**9**	**0**	**951**	**99%**
				95% two-sided Confidence Lower Limit	**98%**

[a] Genotype by bi-directional sequencing; *1/*1 samples are wild-type for *2, *3, and *17.
[b] In order for a sample to be deemed a correct, results of all three genotypes (*2,*3,*17) had to be correct.

Inter-Laboratory Reproducibility Second Pass Tests				
Sample Type	**# Samples Tested**	**# Inconclusive Calls**	**# Incorrect Calls**	**# Correct Calls**
*1/*3	1	0	0	1
*2/*2	1	0	0	1
*2/*17	3	0	0	3
*17/*17	1	0	0	1
Total Samples (all sites, all lots)	**6**	**0**	**0**	**6**

Inter-Laboratory Reproducibility – Final (Combined First and Second Pass)						
Sample Type [a]	**# Samples Tested**	**# Inconclusive Calls**	**# Incorrect Calls**	**# Correct Calls [b]**	**Correct call rate (%)**	**95% two-sided Confidence Lower Limit**
*1/*1	120	0	0	120	100	97
*1/*2	120	0	0	120	100	97
*1/*3	120	0	0	120	100	97
*1/*17	120	0	0	120	100	97
*17/*17	120	0	0	120	100	97
*2/*17	120	2	0	118	98.3	94.1
*2/*2	120	0	0	120	100	97
*2/*3	120	1	0	119	99.2	95.4
Total Samples (all sites, all lots)	**960**	**3**	**0**	**957**	**99.7%**	**99.1%**

[a] Genotype by bi-directional sequencing; *1/*1 samples are wild-type for *2, *3, and *17.
[b] In order for a sample to be deemed a correct, results of all three genotypes (*2,*3,*17) had to be correct.

Test Kit Lot-to-Lot Reproducibility

Inter-Laboratory Reproducibility data was used to assess Lot-to-lot and site-to-site reproducibility using the three independent lots of test kit.

Test Kit Lot-to-Lot Reproducibility – Final (Combined First and Second Pass)							
Test Kit Reagent Lots	**SITE**	**# Samples Tested**	**# Inconclusive Calls**	**# Incorrect Calls**	**# Correct Calls**	**% Correct Call Rate**	**95% two-sided Confidence Lower Limit**
Lot A	**1 & 3**	**320**	**1** [a]	0	**319**	**99.7**	**98.3**
Lot B	**1 & 2**	**320**	**2** [a]	0	**318**	**99.4**	**97.8**
Lot C	**2 & 3**	**320**	**0**	0	**320**	**100**	**98.8**

[a] Three subjects were not available to be re-run after a first pass inconclusive result was obtained; therefore, the inconclusive was applied to the final result.

On the first pass, nine samples (Lot A (3), Lot B (5), Lot C (1)) produced inconclusive results. A second pass test was performed on six of the nine samples, all six results were resolved. The remaining three samples were not available for a second pass test. The first pass inconclusive result was applied to the final result. Overall, the results indicate reagent lots and each site perform equivalently.

1.7.4 Method Comparison

The CYP2C19 *2, *3 and *17 allele genotyping accuracy of the Genomadix Cube CYP2C19 system was evaluated by comparing genotype calls generated by the system and genotypes generated through bi-directional sequencing.

After first pass the Genomadix Cube CYP2C19 platform resulted in a correct call rate of 96% (414/433) with 17 inconclusive results, and two incorrect calls. New swabs that were collected from only those subjects that generated a first pass inconclusive result were tested. The second pass resolved 15 of the 17 inconclusive results. The final correct call to 99% with a 95% two-sided confidence lower limit of 98%.

Method Comparison – First Pass					
Sample Type	**# Unique Samples tested**	**# Inconclusive/No Call**	**# Incorrect calls**	**# Correct calls**	**% Correct call rate**
*1/*1	144	3	0	141	98
*1/*2	124	2	1	120	97
*1/*3	13	1	0	13	100
*1/*17	78	4	0	71	91
*2/*2	24	2	1	23	96
*2/*3	6	2	0	5	83
*2/*17	26	2	0	22	85
*3/*3	1	0	0	1	100
*3/*17	1	0	0	1	100
*17/*17	16	1	0	12	75
Total	**433**	**17**	**2**	**414**	**96%**
				95% two-sided Confidence Lower limit	**93%**

Method Comparison Second Pass Testing				
Sample Type	**# Unique Samples tested**	**# Inconclusive/No Call**	**# Incorrect calls**	**# Correct calls**
*1/*1	3	0	0	3
*1/*2	2	0	0	2
*1/*3	1	0	0	1
*1/*17	4	1	0	3
*2/*2	2	0	0	2
*2/*3	2	1	0	1
*2/*17	2	0	0	2
*17/*17	1	0	0	1
Total	**17**	**2**	**0**	**15**

Method Comparison Final (Combined First and Second Pass)						
Sample Type	# Unique Samples tested	# Inconclusive/No Call	# Incorrect calls	# Correct calls	% Correct call rate	95% two-sided Lower Confidence limit
*1/*1	144	0	0	144	100	97
*1/*2	124	0	1	123	99	97
*1/*3	13	0	0	13	100	77
*1/*17	78	1	0	77	99	93
*2/*2	24	0	1	23	96	80
*2/*3	6	1	0	5	83	44
*2/*17	26	0	0	26	100	87
*3/*3	1	0	0	1	100	21
*3/*17	1	0	0	1	100	21
*17/*17	16	0	0	16	100	81
Total	**433**	**2**	**2**	**429**	**99%**	**98%**

As part of the study, there were two unresolved inconclusive (no call) results, that were due to lack of DNA amplification.

The laboratory sequencing was not completed in advance, and the miscalls were not identified until after the completion of the testing at the site. Miscall investigation would have been required at the time the

Genomadix testing was being completed on site. Root cause not identified. The probable root cause is that the samples were swapped by the operator, however this cannot be confirmed.

Proper sample collection and sample handling are essential for correct result, as well as to avoid errors related to sample misidentification and/or mishandling.

1.7.5 Analytical Sensitivity (Limit of Detection)

The Upper and Lower Limit of detection (LoD) for the Genomadix CYP2C19 System:

Result	Criteria	Buccal Collection	Technique Reference/Rationale	Detection (% agreement)
Lower LoD (LLoD)	The lowest quantity of buccal sample that can be collected on a CYP2C19 swab that can be consistently detected in ≥95% of samples tested.	**Single inside cheek touch**	Technique that will collect the minimum possible amount of buccal sample.	**99%** 117/118, one Inconclusive result
Upper LoD (ULoD)	The highest quantity of buccal sample that can be collected on a CYP2C19 swab that can be consistently detected in ≥95% of samples tested.	**Fifteen (15) up-and-down strokes**	5-fold increase over the IFU technique (5X Instructions for Use (IFU), workflow)	**100%** 30/30

The upper limit of detection was assessed by swabbing 5x (15 up-and-down strokes) the standard workflow (3 up-and-down strokes). The lower limit of detection was assessed by using a single stroke of the swab or a single cheek-touch, where the swab is pressed against the inside of the cheek without a stroke.

Seven different genotypes (*1/*1, *1/*2, *2/*17, *3 containing (*1/*3, *2/*3), *1/*17 and *17/*17) were used to assess the LoD.

If the result of the first test (first pass) generated an inconclusive result, a second set of swabs was collected from that individual using the same collection technique and the test was repeated (second pass). The second pass test is considered the final result.

First pass testing generated a total of nine inconclusive results: one 5x standard workflow, three standard workflow, and six cheek touch samples. New swabs were collected, using the same swabbing method, only for the subjects for whom inconclusive results were obtained.

After second pass testing (one allowable retest), eight of nine samples with associating conditions were resolved, were resolved.

Limit of Detection (LoD) First Pass						
CONDITION	**GENOTYPE**		**# TESTS**	**NO CALL**	**CORRECT RESULTS**	**TOTAL CORRECT**	**CORRECT CALL RATE%**
Original Cheek Touch	*1/*1		5	0	5	18/20	90%
	*1/*3	*3 containing	5	2	0		
	*2/*3			0	3		
	*2/*17		5	0	5		
	*17/*17		5	0	5		
Additional Cheek Touch[a]	*1/*1		27	1	26	94/98	96%
	*1/*2		36	2	34		
	*1/*17		9	0	9		
	*1/*3	*3 containing	4	0	4		
	*2/*3		4	0	4		
	*2/*17		9	0	9		
	*17/*17		9	1	8		
Single Stroke	*1/*1		5	0	5	30/30	100%
	*1/*2		5	0	5		
	*1/*17		5	0	5		
	*1/*3	*3 containing	5	0	2		
	*2/*3			0	3		
	*2/*17		5	0	5		
	*17/*17		5	0	5		
IFU	*1/*1		5	0	5	28/30	93%
	*1/*2		5	0	5		
	*1/*17		5	0	5		
	*1/*3	*3 containing	5	1	1		
	*2/*3			0	3		
	*2/*17		5	1	4		
	*17/*17		5	0	5		
5x IFU	*1/*1		5	1	4	29/30	97%
	*1/*2		5	0	5		
	*1/*17		5	0	5		
	*1/*3	*3 containing	5	0	2		
	*2/*3			0	3		
	*2/*17		5	0	5		
	*17/*17		5	0	5		
TOTAL			**208**	**9**	**199**		

[a] Additional cheek touch samples were tested increasing the sample size to provide confidence on the lower limit of detection.

Limit of Detection (LoD) Second Pass Tests					
CONDITION	**GENOTYPE**		**# TESTS**	**NO CALL**	**CORRECT RESULTS**
Original Cheek Touch	*1/*3	*3 containing	2	**1**	1
	*2/*3		N/A	N/A	N/A
Additional Cheek Touch[a]	*1/*1		1	0	1
	*1/*2		2	0	2
	*17/*17		1	0	1
IFU	*1/*3	*3 containing	1	0	1
	*2/*3		N/A	N/A	N/A
	*2/*17		1	0	1
5x IFU	*1/*1		1	0	1
TOTAL			**9**	**1**	**8**

[a] Additional cheek touch samples were tested increasing the sample size to provide confidence on the lower limit of detection.

Limit of Detection Final (Combined First and Second Pass)							
CONDITION	**GENOTYPE**	**# TESTS**	**NO CALL**	**CORRECT RESULTS**	**FINAL CORRECT**	**CORRECT CALL RATE%**	
Original Cheek Touch	*1/*1	5	0	5	19/20	95%	99%
	*1/*3 *3 containing	5	1	4			
	*2/*3 *3 containing		0				
	*2/*17	5	0	5			
	*17/*17	5	0	5			
Additional Cheek Touch[a]	*1/*1	27	0	27	98/98	100%	
	*1/*2	36	0	36			
	*1/*17	9	0	9			
	*1/*3 *3 containing	4	0	4			
	*2/*3 *3 containing	4	0	4			
	*2/*17	9	0	9			
	*17/*17	9	0	9			
Single Stroke	*1/*1	5	0	5	30/30	100%	
	*1/*2	5	0	5			
	*1/*17	5	0	5			
	*1/*3 *3 containing	5	0	5			
	*2/*3 *3 containing		0				
	*2/*17	5	0	5			
	*17/*17	5	0	5			
IFU	*1/*1	5	0	5	30/30	100%	
	*1/*2	5	0	5			
	*1/*17	5	0	5			
	*1/*3 *3 containing	5	0	5			
	*2/*3 *3 containing		0				
	*2/*17	5	0	5			
	*17/*17	5	0	5			
5x IFU	*1/*1	5	0	5	30/30	100%	
	*1/*2	5	0	5			
	*1/*17	5	0	5			
	*1/*3 *3 containing	5	0	5			
	*2/*3 *3 containing		0				
	*2/*17	5	0	5			
	*17/*17	5	0	5			
TOTAL		**208**	**1**	**207**			

[a] Additional cheek touch samples were tested increasing the sample size to provide confidence on the lower limit of detection.

1.7.6 Interference

Interference from potential endogenous and exogenous interfering substances was evaluated using buccal swab samples collected from *1/*1, *2/*17, *17/*17, *1/*3, and *2/*3 individuals. Genotypes of all individuals were confirmed by bi-directional sequencing prior to initiation of the study. Buccal swab samples were collected from individuals after exposure to the substance (immediately after, no rinsing) or the substance was added to the buccal swab (blood) or the substance was added to the reaction (bacteria).

A total of 16 replicates were tested for each substance. If the result of the first test (first pass) was inconclusive, a second set of swabs was collected from that individual and exposed to the same interfering substance followed by repeat testing (second pass). The second pass test is considered the final result and has been used when calculating the performance characteristics. The interfering substances included in the study are detailed below.

On the first pass, four samples (Toothpaste (2), Sugar solution (1) and Tobacco (1)) produced inconclusive results. New swabs collected only for those four samples that obtained an inconclusive result. A second pass test (one allowable retest) was performed on these samples, all four samples were resolved after the second pass.

No interference detected from any of the exogenous or endogenous substances tested.

Interfering Substances First Pass

Substance		# Samples Tested	# Inconclusive Calls	# Incorrect Calls	# Correct Calls	% Correct Calls
Baking Soda	30 mL, rinse 10 seconds	16	0	0	16	100
Chewing gum	1 piece, chew 1 minute	16	0	0	16	100
Cough Syrup	30 mL, rinse 10 seconds	16	0	0	16	100
Cranberry juice	30 mL, rinse 10 seconds	16	0	0	16	100
Denture paste	3 strips roof of mouth, remove after 5 minutes	16	0	0	16	100
Hard candy	1 piece fully dissolve	16	0	0	16	100
Horse meat	15g, chew 10 seconds	16	0	0	16	100
Mouthwash	20 mL, rinse 10 seconds	16	0	0	16	100
Salt solution	30 mL, rinse 10 seconds	16	0	0	16	100
Sugar solution	30 mL, rinse 10 seconds	16	1	0	15	94
Tobacco	5 inhale and exhale	16	1	0	15	94
Toothpaste	1.9cm brush 2 minutes	16	2	0	14	88
Bacteria (oral)	~ 9 x 10^4 cells added to each reaction tube for each test	16	0	0	16	100
Whole blood	Swab dipped in a 1.7% blood/saliva mixture	16	0	0	16	100
Total		**224**	**4**	**0**	**220**	**98%**

Interfering Substances Second Pass Tests

Substance		# Samples Tested	# Inconclusive Calls	# Incorrect Calls	# Correct Calls
Sugar solution	30 mL, rinse 10 seconds	1	0	0	1
Tobacco	5 inhale and exhale	1	0	0	1
Toothpaste	1.9cm brush 2 minutes	2	0	0	2

Interfering Substances – Final (Combined First and Second Pass)						
Substance		# Samples Tested	# Inconclusive Calls	# Incorrect Calls	# Correct Calls	% Correct Calls
Baking Soda	30 mL, rinse 10 seconds	16	0	0	16	100
Chewing gum	1 piece, chew 1 minute	16	0	0	16	100
Cough Syrup	30 mL, rinse 10 seconds	16	0	0	16	100
Cranberry juice	30 mL, rinse 10 seconds	16	0	0	16	100
Denture paste	3 strips roof of mouth, remove after 5 minutes	16	0	0	16	100
Hard candy	1 piece fully dissolve	16	0	0	16	100
Horse meat	15g, chew 10 seconds	16	0	0	16	100
Mouthwash	20 mL, rinse 10 seconds	16	0	0	16	100
Salt solution	30 mL, rinse 10 seconds	16	0	0	16	100
Sugar solution	30 mL, rinse 10 seconds	16	0	0	16	100
Tobacco	5 inhale and exhale	16	0	0	16	100
Toothpaste	1.9cm brush 2 minutes	16	0	0	16	100
Bacteria (oral)	~ 9 x 104 cells added to reaction	16	0	0	16	100
Whole blood	Swab dipped in a 1.7% blood/saliva mixture	16	0	0	16	100
Total		**224**	**0**	**0**	**224**	**100%**

1.7.7 Swab Stability

Stability studies were conducted to determine the sample stability of the buccal sample on the system Swabs. It was determined that a sample, collected on the swab, can be stored for up to 20 hours at room temperature (18-25°C, 30-70% relative humidity) after collection.

Do not ship buccal swab samples; shipping stability of buccal sample has not been evaluated. It has only been validated to be transported at 18-25°C, 30-70% relative humidity.

1.7.7.1 Swab Stability Testing during Method Comparison Studies

During the method comparison testing, additional swabs were collected from 208 of the participants, and stored at ambient temperature for 21 hours. At 21 hours the swabs were tested following the standard workflow.

Swab Stability Testing during Method Comparison Studies – First Pass					
Genotype	# Tested	# Inconclusive Calls (No Call)	Incorrect Call	Correct Results	% Correct Call Rate
*1/*1	67	0	0	67	100
*1/*2	56	0	0	56	100
*1/*3	4	0	0	4	100
*1/*17	39	0	0	39	100
*2/*2	14	0	0	14	100
*2/*3	3	0	0	3	100
*2/*17	15	0	0	15	100
*3/*17	1	0	0	1	100
*17/*17	9	0	0	9	100
TOTAL	**208**	**0**	**0**	**208**	**100%**
				95% two-sided Confidence Lower limit	**98%**

1.7.8 Test Cartridge Shelf-Life

Shelf-life studies were conducted to determine the expiration date of the CYP2C19 Test Cartridge. Based on the study, when stored at a temperature between -15°C and -80°C, the expiration is 12 months.

1.7.9 Software Verification and Validation

The software for this device was considered as a “moderate” level of concern. This was determined since a failure or latent design flaw could directly or indirectly result in minor injury to the patient or operator through incorrect or delayed information or through the action of a care provider.

Software verification and validation testing was conducted in accordance with established specifications and IEC 62304 and documentation was provided as recommended by FDA Guidance document “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices,” May 11, 2005. Results of executed protocols for the met the acceptance criteria and therefore supports that the system’s embedded software is acceptable for its intended use.

1.7.10 Cybersecurity

The Genomadix Cube CYP2C19 System is intended to be used without being attached to a computer network (either wired or wireless connection) with physical access controls in place. The product does not require a network connection to function in normal use, and functionality is not enhanced by attaching to a network.

Cybersecurity risk management documentation for the System that includes analysis of confidentiality, integrity, and availability for data, information and software related to the System. For each identified threat and vulnerability risk event scenario, risk assessment of impact to confidentiality integrity, and availability was performed and documented. Appropriate risk mitigation controls have been implemented.

1.7.11 Electrical Safety and Electromagnetic Compatibility (EMC)

The System underwent electrical safety and EMC evaluation. Results of this evaluation demonstrated that the System complies with electrical safety and EMC requirements.

2 Conclusion

The Genomadix Cube CYP2C19 System has the same intended use and clinical application as the predicate device. The difference in technological characteristics, have been addressed through risk control measures to provide reasonable assurance of the safety and effectiveness of the Genomadix System. Based on the performance testing and data provided in this pre-market notification, the subject and predicate device supports a substantial equivalence decision.