510(K) Summary

510(k) Number:

K120466: Verigene® CYP2C19 Nucleic Acid Test (CYP2C19)

NOV 6 2012

Summary Preparation Date:

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Submitted by:

Nanosphere, Inc.
4088 Commercial Avenue
Northbrook, IL 60062
Phone: 847-400-9000
Fax: 847-400-9176

Contact:

Mark A. Del Vecchio
Vice President, Regulatory Affairs

Proprietary Names:

For the instrument:

Verigene® System

For the assay:

Verigene® CYP2C19 Nucleic Acid Test (CYP2C19 Test)

Common Names:

For the instrument:

Bench-top molecular diagnostics workstation

For the assay:

Cytochrome P450 CYP2C19 Drug Metabolizing Test

Regulatory Information:

Regulation section:

862.3360 Drug Metabolizing Enzyme Genotyping System
862.2570 Instrumentation for Clinical Multiplex Test Systems

Classification:

Class II

Panel:

Toxicology (91)
Chemistry (75)

Product Code(s):

NTI Drug Metabolizing Enzyme Genotyping System
NSU Instrumentation for Clinical Multiplex Test Systems
Other codes used by predicate devices:
None

Predicate Device(s):

INFINITI®CYP2C19 Assay (K101683)

Indications for Use:

The Verigene® CYP2C19 Nucleic Acid Test (CYP2C19 Test), performed using the sample-to-result Verigene System, is a qualitative multiplexed *in vitro* diagnostic test for the simultaneous detection and identification of an individual's CYP450 2C19 genotype in genomic deoxyribonucleic acid (DNA) obtained from EDTA-anticoagulated whole blood samples. The Verigene CYP2C19 Nucleic Acid Test (CYP2C19 Test) is indicated for use in clinical laboratories upon prescription by the attending physician as an aid to clinicians in determining therapeutic strategy for therapeutics that are metabolized by the CYP450 2C19 gene product, specifically *2, *3, and *17. The Verigene CYP2C19 Nucleic Acid Test (CYP2C19 Test) is not indicated to be used to predict drug response or non-response.

Technological Characteristics:

The Verigene® System is comprised of test consumables and shared instrumentation. All Verigene tests are formatted in self-contained test-specific Verigene Test Cartridges which serve to analyze a nucleic acid sample that is presented to them. Nucleic acids are prepared directly from a whole blood specimen using magnetic glass particles and input automatically into a Test Cartridge inside the Verigene Processor *SP*. Test progress is tracked and directed by the Verigene Reader instrument, which serves as a central control unit for each Verigene System.

Genomic DNA is extracted from the white blood cells in a whole blood specimen, fragmented and denatured. This fragmented, single-stranded genomic DNA hybridizes to complementary sequence-specific DNA oligonucleotides, known as capture oligonucleotides, arrayed on the surface of a substrate (glass slide). A second DNA oligonucleotide is then hybridized to the captured genomic DNA that was captured initially. This oligonucleotide is known as a mediator oligonucleotide containing two sequence domains: one domain is complementary to the genomic DNA target and a second domain is complementary to a common oligonucleotide attached to a signal generating gold nanoparticle probe. After washing away any DNA not affixed to the captures, the probe is exposed to the captured mediator/target compound where it hybridizes to any captured mediators. Presence of the gold nanoparticle probes at a particular location on the substrate is assessed optically.

The Verigene CYP2C19 Nucleic Acid Test is designed to detect and genotype the CYP450 2C19 *2, *3 and *17 alleles. The test report lists the alleles and provides which genotype was detected in the specimen. The CYP2C19 Test algorithm automatically calculates each of the allele results using a preset normalized ratio of the signal of wild type capture locations on the microarray to the mutant capture locations on the microarray.

Substantial Equivalence:

The Verigene® CYP2C19 Nucleic Acid Test (CYP2C19) has the same Intended Use and Indications for Use, similar technological and performance characteristics, and similar principles of operation as its predicate device, the INFINITI®CYP2C19 Assay (K101683), that the Food and Drug Administration ("FDA") has cleared for the identification of a patient's CYP450 2C19 genotype in genomic deoxyribonucleic acid (DNA) obtained from EDTA-anticoagulated whole blood samples (see **Table 1**). The INFINITI CYP2C19 Assay is a qualitative *in vitro* assay for use in clinical laboratories upon prescription by the attending physician and is indicated for use as an aid to clinicians in determining therapeutic strategy for therapeutics that are metabolized by CYP450 enzymes known to be affected by mutations in the *2, *3 and *17 alleles of the CYP2C19 gene. The INFINITI CYP2C19 Assay (K101683) is not indicated to be used to predict drug response or non-response. The minor differences between the CYP2C19 test and its predicate device raise no new issues of safety or effectiveness. The analytical and clinical performance data demonstrate that the CYP2C19 test is as safe and effective as the predicate device. Therefore, the Verigene CYP2C19 Nucleic Acid Test is substantially equivalent to the INFINITI CYP2C19 Assay.

Table 1: Comparative Characteristics: CYP2C19 Test and Predicate Device

Items	*Device*	*Predicate*
	Verigene CYP2C19 Test	**INFINITI CYP2C19 Assay**
510(k)#	K120466	K101683
Regulations	862.3360 and 862.2570	Same
Product Code	NTI, NSU	Same
Device Class	II	Same
Intended Use	Identification of an individual's CYP450 2C19 genotype	Same
Indications for Use	To aid in determining therapeutic strategy for therapeutics metabolized by the CYP450 2C19 gene product, specifically *2, *3, and *17 alleles.	Same
Warnings and Precautions	For use in clinical laboratories upon prescription by the attending physician	Same
Contraindication (s)	Assay is not intended to be used to predict drug response or non-response.	Same
Test Cartridge	Disposable single-use, multi- chambered fluidic cartridge.	Same
Sample Type	EDTA-anticoagulated whole blood	Same
Sample Prep	On-board, automated DNA extraction	Same
Quality control	Internal procedural/instrument quality controls; Internal Negative Control, Sample processing control, external positive and negative assay controls	Same
Interpretation of Results	Diagnostic Software/Decision Algorithm	Same
Target Mutations	*2, *3, and *17 genotype of CYP 2C19	Same
Type of Test	Genotyping microarray	Same
Detection Method	Gold/Ag nanoparticle probe detection of DNA on complementary oligo- microarray	Measures fluorescent signals of labeled DNA target hybridized to the microarray.
DNA Extraction Method	Automated DNA extraction with "blood sample to result system"	Manual, "off-line" DNA extraction
Sample Carry-over	None observed	Same
Interference	None observed for bilirubin, triglyceride, cholesterol, and albumin	Same
Precision Initial Call Rate Final Call Rate Agreement vs BDS	 97.7% 100% 100%	Not Done
Reproducibility Initial Call Rate Final Call Rate Agreement vs BDS	 96.9% 99.6% 99.6%	 96.5% 100% 99.8%
Method Comparison Initial Call Rate Final Call Rate Agreement vs BDS	 94.8% 99.9% 99.6%	 98.1% 100% 100%

Performance Data Summary - Analytical Testing

Analytical Sensitivity / Limit of Detection (LOD)

To evaluate the upper and lower limits of the assay sample volume between which the CYP2C19 Test performs properly, seven individual whole blood samples, each containing a different genotype, *1/*1, *1/*2, *2/*2, *2/*17, *1/*3, *1/*17, and *17/*17, were tested in replicates of 40 at sample input volumes of 800µL, 900µL, 1000µL, 1100µL, and 1200µL. The study demonstrated that the CYP2C19 Test detected each genotype consistently (initial call rate >90%) and accurately (100% vs. BDS) for all genotypes tested between the specimen volume range of 1000 ± 200µL (800µL – 1200µL). These results establish 1.0 ± 0.1mL of whole blood as the sample volume tolerance for the assay. The ability of the CYP2C19 test to consistently detect the genotype of a specimen will be negatively impacted at whole blood sample input volumes of less than 750µL.

Interference Testing

The potential inhibitory effects of substances that may be present in whole blood were evaluated at biologically relevant but elevated concentrations, by individually adding albumin (@6000 mg/dL), bilirubin (conjugated and unconjugated @20 mg/dL), triglycerides (@3000 mg/dL), and cholesterol (@500 mg/dL) directly into EDTA-anticoagulated whole blood samples, each individually containing genotypes *1/*1, *1/*2, *2/*2, *2/*17, *1/*3, *1/*17, and *17/*17. A total of 30 replicates per specimen containing each interfering substance were tested and the results compared to unspiked control samples. In the presence of these substances, each genotype was detected consistently with 100% accuracy vs. BDS, demonstrating that these substances do not interfere with the CYP2C19 Test.

Table 2: Interfering Substance Testing - Initial and Final Call Rates by Genotype

Genotype	No. Tested	Interfering Substance	Reps per Interferent	Initial Results					Final Results				
				No. of Genotype Calls		No Calls	% Agreement	95% One-sided CI LL	No. of Genotype Calls		No Calls	% Agreement	95% One-sided CI LL
				Correct	Incorrect				Correct	Incorrect			
*1/*1	1	Control	30	29	0	1	97	85.1	30	0	0	100	90.5
		Cholesterol	30	28	0	2	93	80.5	30	0	0	100	90.5
		Triglycerides	30	29	0	1	97	85.1	30	0	0	100	90.5
		Unconj. Bilirubin	30	29	0	1	97	85.1	30	0	0	100	90.5
		Conj. Bilirubin	30	29	0	1	97	85.1	30	0	0	100	90.5
		Albumin	30	28	0	2	93	80.5	30	0	0	100	90.5
		TOTAL	180	172	0	8	96	92.1	180	0	0	100	98.4
*1/*2	1	Control	30	30	0	0	100	90.5	30	0	0	100	90.5
		Cholesterol	30	29	0	1	97	85.1	30	0	0	100	90.5
		Triglycerides	30	30	0	0	100	90.5	30	0	0	100	90.5
		Unconj. Bilirubin	30	29	0	1	97	85.1	30	0	0	100	90.5
		Conj. Bilirubin	30	30	0	0	100	90.5	30	0	0	100	90.5
		Albumin	30	30	0	0	100	90.5	30	0	0	100	90.5
		TOTAL	180	178	0	2	99	96.5	180	0	0	100	98.4
*1/*3	1	Control	30	30	0	0	100	90.5	30	0	0	100	90.5
		Cholesterol	30	30	0	0	100	90.5	30	0	0	100	90.5
		Triglycerides	30	28	0	2	93	80.5	30	0	0	100	90.5
		Unconj. Bilirubin	30	30	0	0	100	90.5	30	0	0	100	90.5
		Conj. Bilirubin	30	30	0	0	100	90.5	30	0	0	100	90.5
		Albumin	30	27	0	3	90	76.1	29	0	1	97	85.1
		TOTAL	180	175	0	5	97	94.3	179	0	1	99	97.4
*1/*17	1	Control	30	30	0	0	100	90.5	30	0	0	100	90.5
		Cholesterol	30	30	0	0	100	90.5	30	0	0	100	90.5
		Triglycerides	30	27	0	3	90	76.1	30	0	0	100	90.5
		Unconj. Bilirubin	30	28	0	2	93	80.5	30	0	0	100	90.5
		Conj. Bilirubin	30	26	0	4	87	72.0	30	0	0	100	90.5
		Albumin	30	29	0	1	97	85.1	30	0	0	100	90.5
		TOTAL	180	170	0	10	94	90.8	180	0	0	100	98.4
*2/*2	1	Control	30	30	0	0	100	90.5	30	0	0	100	90.5
		Cholesterol	30	29	0	1	97	85.1	30	0	0	100	90.5
		Triglycerides	30	30	0	0	100	90.5	30	0	0	100	90.5
		Unconj. Bilirubin	30	30	0	0	100	90.5	30	0	0	100	90.5
		Conj. Bilirubin	30	30	0	0	100	90.5	30	0	0	100	90.5
		Albumin	30	30	0	0	100	90.5	30	0	0	100	90.5
		TOTAL	180	179	0	1	99	97.4	180	0	0	100	98.4
*2/*17	1	Control	30	27	0	3	90	76.1	30	0	0	100	90.5
		Cholesterol	30	28	0	2	93	80.5	30	0	0	100	90.5
		Triglycerides	30	27	0	3	90	76.1	30	0	0	100	90.5
		Unconj. Bilirubin	30	29	0	1	97	85.1	30	0	0	100	90.5
		Conj. Bilirubin	30	28	0	2	93	80.5	29	0	1	97	85.1
		Albumin	30	27	0	3	90	76.1	30	0	0	100	90.5
		TOTAL	180	166	0	14	92	88.1	179	0	1	99	97.4
*17/*17	1	Control	30	29	0	1	97	85.1	29	0	1	97	85.1
		Cholesterol	30	28	0	2	93	80.5	29	0	1	97	85.1
		Triglycerides	30	29	0	1	97	85.1	30	0	0	100	90.5
		Unconj. Bilirubin	30	30	0	0	100	90.5	30	0	0	100	90.5
		Conj. Bilirubin	30	30	0	0	100	90.5	30	0	0	100	90.5
		Albumin	30	30	0	0	100	90.5	30	0	0	100	90.5
		TOTAL	180	176	0	4	98	95.0	178	0	2	99	96.5
ALL			1260	1216	0	44	96.5	95.5	1256	0	4	99.7	99.3

Specimen Stability Study

The stability of freshly-collected whole blood samples, stored refrigerated for up to 15 days following collection, was evaluated by testing with the CYP2C19 Test. Aliquots of thirty-five (35) EDTA whole blood samples, containing individually genotypes *1/*1 (n=16), *1/*2 (n=4), *2/*2 (n=1), *1/*17 (n=11), and *17/*17 (n=3), were tested once at 5, 10, 12, and 15 day time points with the CYP2C19 Test and the extracted DNA concentration and purity measured for each sample. No signs of degradation (e.g., no decrease in extracted DNA concentration and/or purity, observed daily call rate for all 35 samples tested ≥97%, and genotype accuracy of 100%) were observed for any sample during the study, establishing 10 days at refrigerated storage (2 to 8°C) as the whole blood specimen stability claim for the CYP2C19 Test.

Carry-over / Cross-contamination

In order to demonstrate that the CYP2C19 Test, when performed on the Verigene System, is not susceptible to sample carry-over or cross-contamination, testing of whole blood specimens containing different genotypes was performed sequentially on ten Verigene instruments (e.g.;*1/*2, followed by *1/*1, then *1/*17, then *1/*1); this testing was repeated in triplicate. Genotyping accuracy was 100% and no evidence of carryover and/or cross-contamination was observed (initial call rates >93% for each of the three genotypes tested.)

Precision

Precision of the CYP2C19 Test was evaluated by testing eight unique whole blood specimens (containing genotypes *1/*1, *1/*2, *2/*2, *2/*17, *1/*3 (2 tested), *1/*17, and *17/*17) in duplicate twice daily by two operators for twelve non-consecutive days at one testing site. This testing regimen generated a total of forty-eight (48) replicates per specimen and an overall total of 384 data points. Of the 384 samples tested, the percent agreement for all panel members as compared to bi-directional sequencing was 100% (384/384). There were nine (9) "No Calls" in the study for an initial call rate of 97.7% (375/384). All nine of these samples were repeat tested successfully for a final call rate of 100% (384/384).

Table 3: CYP2C19 Test Precision Study Results

Genotype	No. Tested	Reps per Sample	Initial Results					Final Results				
			No. of Genotype Calls		No Calls	Agreement	95% One-sided CI LL	No. of Genotype Calls		No Calls	Agreement	95% One-sided CI LL
			Correct	Incorrect				Correct	Incorrect			
*1/*1	1	48	47	0	1	97.9	90.5	48	0	0	100	94.0
*1/*2	1	48	47	0	1	97.9	90.5	48	0	0	100	94.0
*1/*3	1	48	46	0	2	95.8	87.5	48	0	0	100	94.0
*1/*3	1	48	46	0	2	95.8	87.5	48	0	0	100	94.0
*1/*17	1	48	47	0	1	97.9	90.5	48	0	0	100	94.0
*2/*2	1	48	48	0	0	100	94.0	48	0	0	100	94.0
*2/*17	1	48	47	0	1	97.9	90.5	48	0	0	100	94.0
*17/*17	1	48	47	0	1	97.9	90.5	48	0	0	100	94.0
ALL	***8***	***384***	***375***	***0***	***9***	***97.7***	***96.0***	***384***	***0***	***0***	***100***	***99.2***

Performance Data Summary - Clinical Testing

Reproducibility

Reproducibility of the CYP2C19 Test was evaluated at three sites (two external and one internal) using the same eight-member panel as for the Precision Study. These eight specimens were tested in duplicate twice daily by two operators for five (5) non-consecutive days. This testing regimen generated a total of sixty (60) replicates (20 replicates/site) per specimen for an overall total of 480 data points. A summary of the Reproducibility Study results stratified by investigational site is provided in Table 7. There were fifteen (15) initial "No Calls" in the study for an initial call rate of 96.9% (465/480). Thirteen (13) of these samples were repeat tested successfully for a final call rate of 99.6% (478/480). Considering the two final "No Call" results as discordant results, the percent agreement for all panel members as compared to bi-directional sequencing was 99.6% (478/480).

Table 4: CYP2C19 Test Reproducibility Study Results

Genotype	No. Tested	Reps per Sample	Initial Results					Final Results				
			No. of Genotype Calls		No Calls	Agreement	95% One-sided CI LL	No. of Genotype Calls		No Calls	Agreement	95% One-sided CI LL
			Correct	Incorrect				Correct	Incorrect			
*1/*1	1	60	59	0	1	98.3	92.3	60	0	0	100	95.1
*1/*2	1	60	59	0	1	98.3	92.3	60	0	0	100	95.1
*1/*3	1	60	56	0	4	93.3	85.4	60	0	0	100	95.1
*1/*3	1	60	57	0	3	95.0	87.6	59	0	1	98.3	92.3
*1/*17	1	60	59	0	1	98.3	92.3	60	0	0	100	95.1
*2/*2	1	60	59	0	1	98.3	92.3	60	0	0	100	95.1
*2/*17	1	60	57	0	3	95.0	87.6	59	0	1	98.3	92.3
*17/*17	1	60	59	0	1	98.3	92.3	60	0	0	100	95.1
ALL	8	**480**	**465**	**0**	**15**	**96.9**	**95.2**	**478**	**0**	**2**	**99.6**	**98.7**

Method Comparison Study

A total of 670 unique human whole blood samples, collected in EDTA, were tested at three sites using the Verigene CYP2C19 Nucleic Acid Test. **Table 5** provides agreement with bi-directional sequencing and the number of correct calls observed in the study. **Table 6** shows the initial and final call rates at each of the sites and the combined statistics for each, in addition to agreement with bi-directional sequencing. There were 35 initial no calls of which 34 were successfully repeated. Therefore the initial call rate was 94.8% (635/670) and the final call rate was 99.9% (669/670).

Table 5: Method Comparison Results: Agreement with bi-directional sequencing (n=670)

Genotype [a]	*No. Tested*	*Reps per Sample*	*No. Correct Genotype Calls*	*No. Incorrect Calls*	*No Calls*	*Agreement*	*95% Two-sided Confidence Interval Lower Limit*
*1 / *1 [b]	260	1	260	0	0	100%	98.6%
*1 / *2	177	1	176	0	1[c]	99.4%	96.9%
*1 / *3	24	1	23	1	0	95.8%	78.9%
*1 / *17	114	1	113	1	0	99.1%	95.2%
*2 / *2	32	1	32	0	0	100%	89.1%
*2 / *3	13	1	13	0	0	100%	75.3%
*2 / *17	30	1	30	0	0	100%	88.4%
*3 / *17	1	1	1	0	0	100%	2.5%
*3 / *3	1	1	1	0	0	100%	2.5%
*17 / *17	18	1	18	0	0	100%	81.5%
Total	***670***	***1***	***667***	***2***[c]	***1***	***99.6%***	***98.7%***

a) Genotype determined by bi-directional sequencing
b) *1/*1 samples are inferred if they are wild-type for *2, *3 and *17
c) CYP2C19 result initial and final no-call; BDS result *1/*2.

Table 6: Method Comparison Results, Initial and Final Call Rates and Accuracy by Site and Genotype

	Call Rate Per Genotype (95% Two-Sided Confidence Interval)								*Agreement with Reference Method*
	Site 1[a]		*Site 2*[b]		*Site 3*[c]		*All Sites*		*Bi-Directional Sequencing Result*
n=	*281*		*264*		*125*		*670*		
Genotype	*Initial*	*Final*	*Initial*	*Final*	*Initial*	*Final*	*Initial*	*Final*	
**1/*1*	100% 113/113 (96.8-100)	100% 113/113 (96.8-100)	94.9% 92/97 (88.4-98.3)	100% 97/97 (96.3-100)	92.0% 46/50 (80.8-97.8)	100% 50/50 (92.9-100)	96.5% 251/260 (93.5-98.4)	100% 260/260 (98.6-100)	100% 260/260 (98.6-100)
**1/*2*	95.9% 70/73 (88.5–99.1)	98.6% 72/73 (92.6–99.9)	91.3% 63/69 (82.0–96.7)	100% 69/69 (94.8–100)	94.4% 34/36 (91.3–99.3)	100% 36/36 (90.3–100)	93.8% 167/178 (89.2-96.9)	99.4% 177/178 (96.9-99.9)	99.4% 176/177[d] (96.9-99.9)
**1/*3*	100% 8/8 (63.1-100)	100% 8/8 (63.1-100)	88.9% 8/9 (51.6-99.7)	100% 9/9 (66.4-99.9)	100% 6/6 (54.1-100)	100% 6/6 (54.1-100)	95.7% 22/23 (78.1-99.9)	100% 23/23 (85.2-100)	95.8% 23/24 (78.9-99.9)
**1/*17*	96.2% 51/53 (87.0–99.5)	100% 53/53 (93.3–100)	93.0% 40/43 (80.9–98.5)	100% 43/43 (91.8–100)	100% 17/17 (90.5–100)	100% 17/17 (90.5–100)	95.6% 108/113 (90.0-98.6)	100% 113/113 (96.8-100)	99.1% 113/114 (95.2-99.9)
**2/*2*	100% 11/11 (71.5-100)	100% 11/11 (71.5-100)	100% 16/16 (79.4-100)	100% 16/16 (79.4-100)	100% 5/5 (47.8-100)	100% 5/5 (47.8-100)	100% 32/32 (89.1-100)	100% 32/32 (89.1-100)	100% 32/32 (89.1-100)
**2/*3*	100% 3/3 (29.2-100)	100% 3/3 (29.2-100)	100% 5/5 (47.8-100)	100% 5/5 (47.8-100)	80.0% 4/5 (28.4-99.5)	100% 5/5 (47.8-100)	92.3% 12/13 (64.0-99.8)	100% 13/13 (75.3-100)	100% 13/13 (75.3-100)
**2/*17*	83.3% 10/12 (51.6–97.9)	100% 12/12 (73.5–100)	85.7% 12/14 (57.2–98.2)	100% 14/14 (76.8–100)	75.0% 3/4 (19.4–99.4)	100% 4/4 (39.8–100)	83.3% 25/30 (65.3-94.4)	100% 30/30 (88.4-100)	100% 30/30 (88.4-100)
**3/*17*	0% 0/1 (0–97.5)	100% 1/1 (2.5–100)	-	-	-	-	0% 0/1 (0–97.5)	100% 1/1 (2.5–100)	100% 1/1 (2.5–100)
**3/*3*	100% 1/1 (2.5–100)	100% 1/1 (2.5–100)	-	-	100% 1/1 (2.5–100)	100% 1/1 (2.5–100)	100% 2/2 (15.8-100)	100% 2/2 (15.8-100)	100.0% 1/1[c] (2.5-100)
**17/*17*	100% 6/6 (54.1-100)	100% 6/6 (54.1-100)	81.8% 9/11 (48.2-97.7)	100% 11/11 (71.5-100)	100% 1/1 (2.5–100)	100% 1/1 (2.5–100)	88.9% 16/18 (65.3-98.6)	100% 18/18 (81.5-100)	100% 18/18 (81.5-100)
Total By Site	**97.2% 273/281 (94.5-98.8)**	**99.6% 280/281 (98.0-99.9)**	**92.8% 245/264 (89.0-95.6)**	**100% 264/264 (98.6-100)**	**93.6% 117/125 (87.8-97.2)**	**100% 125/125 (97.1-100)**	***94.8% 635/670 (92.8-96.3)***	***99.9% 669/670 (99.2-100)***	***99.6% 667/670 (98.7-99.9)***

(a) 8 samples - "no-call" repeat testing of two *1/*17, three *1/*2 two *2/*17, and one *3/*17 genotypes.
(b) 19 samples - "no-call" repeat testing of five *1/*1, six *1/*2, one *1/*3, three *1/*17, two *2/*17, and two *17/*17genotypes.
(c) 8 samples - "no-call" repeat testing of four *1/*1, two *1/*2, one *2/*3, and one *2/*17 genotypes.
(d) CYP2C19 result initial and final no-call; BDS result *1/*2.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

Letter date: November 6, 2012

Nanosphere, Inc.
c/o Mark A. Del Vecchio
4088 Commercial Avenue
Northbrook, IL 60062

Re: k120466
Trade Name: Verigene® CYP2C19 Nucleic Acid Test (CYP2C19)
Regulation Number: 21 CFR §862.3360
Regulation Name: Drug Metabolizing enzyme genotyping system
Regulatory Class: Class II
Product Codes: NTI, NSU
Dated: September 20, 2012
Received: September 21, 2012

Dear Mr. Del Vecchio:

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. 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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if

applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson

Digitally signed by Carol C. Benson
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Carol C. Benson, 0.9.2342.19200300.100.1.1=1300086490
Date: 2012.11.06 14:51:34 -05'00'

for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics and
Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use Statement

510(k) Number (if known): K120466

Device Name: Verigene® CYP2C19 Nucleic Acid Test (CYP2C19 Test)

Indications for Use:

The Verigene® CYP2C19 Nucleic Acid Test (CYP2C19 Test), performed using the sample-to-result Verigene System, is a qualitative multiplexed *in vitro* diagnostic test for the simultaneous detection and identification of an individual's CYP450 2C19 genotype in genomic deoxyribonucleic acid (DNA) obtained from EDTA-anticoagulated whole blood samples. The Verigene CYP2C19 Nucleic Acid Test (CYP2C19 Test) is indicated for use in clinical laboratories upon prescription by the attending physician as an aid to clinicians in determining therapeutic strategy for therapeutics that are metabolized by the CYP450 2C19 gene product, specifically *2, *3, and *17. The Verigene CYP2C19 Nucleic Acid Test (CYP2C19 Test) is not indicated to be used to predict drug response or non-response.

Prescription Use ✓ (Part 21 CFR 801 Subpart D) and/or Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIR)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K120466