OCT 1 1 2007

510(k) Summary

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1900 and CFR 807.92.

510(k) number:	K070597
Summary preparation date:	October 5, 2007
Submitted by:	Nanosphere, Inc. 4088 Commercial Avenue Northbrook, IL 60062 Phone: 847-400-9000 Fax: 847-400-9199
Contact:	Sue Kent – Manager, Clinical & Regulatory Affairs
Proprietary names:	*For instrument:* Verigene® System *For the assays:* Verigene HC Nucleic Acid Test Verigene *F5 / F2 / MTHFR* Nucleic Acid Test Verigene *F5 / F2* Nucleic Acid Test Verigene *F2* Nucleic Acid Test Verigene *F5* Nucleic Acid Test Verigene *MTHFR* Nucleic Acid Test
Common names:	*For the instrument:* Bench-top molecular diagnostics workstation *For the assays:* *F2*, *FII*, Factor II, coagulation factor II, prothrombin *F5*, *FV*, Factor V, coagulation factor V *MTHFR*, methylenetetrahydrofolate reductase Hypercoagulation panel HC panel
Device descriptions:	The Verigene System is an *in vitro* diagnostic device for processing and genotyping multiple genes in a DNA sample. The Verigene System consists of two instruments, the Verigene Processor and the Verigene Reader, and utilizes single-use, disposable Test Cartridges to process and genotype multiple genes in a DNA sample in approximately 1½ hours. Clinicians use one or more of the three genes (*F5, F2, MTHFR*) and their associated single nucleotide polymorphisms (SNPs) to help diagnose patients' hereditary contributory factors in forming blood clots (thrombi). On the Verigene System, hypercoagulation testing can include one or more of three genotypes that are associated with hypercoagulation (i.e., thrombophilia). These tests use DNA, extracted from human blood, to detect certain genetic mutations (SNPs).

The analysis sequence is the same for each of the three tests (i.e., *F2, F5, MTHFR*). After extracted and purified DNA, mixed with hybridization buffer, is loaded into the sample well of the Test Cartridge, it is ready for processing and is inserted into the Verigene Processor. An internal barcode reader reads the cartridge ID and sends the information to the Verigene Reader. From this information, the Verigene Reader establishes the hybridization parameters and starts the hybridization process.

The genotyping process occurs with a hybridization of the target analyte to a synthetic gene-specific oligonucleotide capture strand on the Test Cartridge's substrate. A synthetic mediator target-specific oligonucleotide is included with the test-specific sample buffer to form a hybridization "sandwich" with the gene sequence of interest. Washing steps following the target hybridization remove the unbound DNA from the hybridization chamber. A probe, composed of a gold nanoparticle with covalently bound oligonucleotides complementary to a sequence on the intermediate oligonucleotide, is introduced after the target wash. After the probe hybridization is completed, a series of washing steps remove the unbound probe from the hybridization chamber. A two-part signal enhancement reagent is added to the hybridization chamber and reacts with the gold nanoparticle to amplify the signal for the Verigene Reader scanning and analysis.

Upon completion of the genotyping process, the user removes the Test Cartridge from the Verigene Processor which is now ready for the next test.

Once the reagent portion of the Test Cartridge is removed by the user, the substrate is inserted into the Verigene Reader. The Verigene Reader illuminates the signal-enhanced nanoparticles specifically bound to either the wild type or mutant captures for the gene. A photosensor reads the relative brightness of each spot and the Verigene Reader outputs a result based on relative levels of brightness of the wild type to mutant signals.

Intended uses:

- The **Verigene® System** is a bench-top molecular diagnostics workstation that automates the *in vitro* diagnostic analysis and detection of nucleic acids using gold nanoparticle probe technology. The Verigene System is intended to be used by experienced laboratory professionals with training on basic laboratory techniques and on the use of the system components.
- The **Verigene *F5* Nucleic Acid Test** is an *in vitro* diagnostic for the detection and genotyping of a single point mutation (G to A at position 1691; also known as Factor V Leiden) of the human Factor V gene (*F5*; Coagulation Factor V gene) in patients with suspected thrombophilia, from isolated genomic DNA obtained from whole blood samples. The test is intended to be used on the Verigene System.
- The **Verigene *F2* Nucleic Acid Test** is an *in vitro* diagnostic for the detection and genotyping of a single point mutation (G to A at position 20210) of the human Factor II gene (*F2*; prothrombin gene) in patients with suspected thrombophilia, from isolated genomic DNA obtained from whole blood samples. The test is intended to be used on the Verigene System.
- The **Verigene *MTHFR* Nucleic Acid Test** is an *in vitro* diagnostic for the detection and genotyping of a single point mutation (C to T at position 677) of the human 5,10 methylenetetrahydrofolate reductase gene (*MTHFR*) in patients with suspected thrombophilia, from isolated genomic DNA obtained from whole blood samples. The test is intended to be used on the Verigene System.

Predicate devices:

For the instrument: Roche Diagnostics Corporation LightCycler® Instrument (K033734)

For the assays: Roche Diagnostics Corporation Factor V Leiden Kit (K033607)
Roche Diagnostics Corporation Factor II (Prothrombin) G20210A Kit (K033612)

Comparison to Technological Features of the Predicate Device

Characteristic	Verigene System	LightCycler Instrument
Enzymatic manipulation of sample	No (chemical amplification of reporter signal)	Yes (DNA amplification via PCR)
Detection procedure	Single-image sensor where nanoparticles are illuminated using a fixed-wavelength light source	Optical detection of stimulated fluorescence
Heating method	1) Sonication horn for sample denaturation 2) Temperature-controlled heat block in contact with substrate	Hot air cycling with glass capillaries
Detection chemistry	SNP discrimination via oligonucleotide probes; detection via evanescent wave light scatter with nanoparticles	Paired hybridization probes using fluorescence resonance energy transfer (FRET)
Primary operational components	Integrated hybridization/ washing for walkaway assay hybridization and detection. Automated array image acquisition and results interpretation.	Integrated thermocycler and microvolume fluorimeter for walkaway PCR amplification and detection.
Specimen type	Purified nucleic acids	Purified nucleic acids
Specimen preparation	DNA isolation performed off-line. Fragmentation of DNA performed onboard.	Performed off line
Sample positions	4 – 32	32
Sample size	25 µl	10-20 µL in glass capillaries
Number of optical detection channels	One fixed-wavelength imager	Three with fixed wavelengths (530 nm, 640 nm, 710 nm)
Analysis Time	2 minutes	Detection occurs at defined intervals during PCR cycle and can be viewed in real-time
User interface	Embedded software in closed system, integrated graphical user interface.	PC with instrument-specific software (LightCycler version 3.5 or higher)

Performance characteristics for Verigene *F5 / F2 / MTHFR* Nucleic Acid Tests:

Reproducibility Study #1:

Three DNA samples, that had been whole genome amplified, were tested in duplicate twice per day by two operators at each of three test sites. Six lots of test cartridges were utilized (two lots at each site). Site 1 performed this testing for 10 non-consecutive days; Sites 2 and 3 performed the testing for 5 non-consecutive days.

F5	Site	Correct Calls (%)	No Calls (%)	Mis-calls (%)
Operator A	1	117 (99.2%)*	1 (0.8%)	0 (0.0%)
Operator B		114 (99.1%)*	1 (0.9%)	0 (0.0%)
Operator C	2	59 (98.3%)	1 (1.7%)	0 (0.0%)
Operator D		59 (98.3%)	1 (1.7%)	0 (0.0%)
Operator E	3	58 (100.0%)*	0 (0.0%)	0 (0.0%)
Operator F		57 (96.6%)*	2 (3.4%)	0 (0.0%)

F2	Site	Correct Calls (%)	No Calls (%)	Mis-calls (%)
Operator A	1	117 (99.2%)*	1 (0.8%)	0 (0.0%)
Operator B		114 (99.1%)*	1 (0.9%)	0 (0.0%)
Operator C	2	58 (96.7%)	2 (3.3%)	0 (0.0%)
Operator D		59 (98.3%)	1 (1.7%)	0 (0.0%)
Operator E	3	58 (100.0%)*	0 (0.0%)	0 (0.0%)
Operator F		55 (93.2%)*	4 (6.8%)	0 (0.0%)

MTHFR	Site	Correct Calls (%)	No Calls (%)	Mis-calls (%)
Operator A	1	117 (99.2%)*	1 (0.8%)	0 (0.0%)
Operator B		113 (98.3%)*	2 (1.7%)	0 (0.0%)
Operator C	2	58 (96.7%)	2 (3.3%)	0 (0.0%)
Operator D		58 (96.7%)	2 (3.3%)	0 (0.0%)
Operator E	3	58 (100.0%)*	0 (0.0%)	0 (0.0%)
Operator F		56 (94.9%)*	3 (5.1%)	0 (0.0%)

*Ten cartridges (7 at Site 1 and 3 at Site 3) failed to run.

Reproducibility Study #2:

A subsequent reproducibility testing included 4 studies, each using a different DNA sample extracted from fresh whole blood by the operators at 3 sites.

Study Description	Summary of Results			
	3 Sites	***F5***	***F2***	***MTHFR***
Each of the three test sites ran the same sample in duplicate.	Site 1	HET	HET	HET
		HET	HET	HET
	Site 2	HET	HET	HET
		HET	HET	HET
	Site 3	HET	HET	HET
		HET	HET	HET

One operator analyzed the same sample in duplicate each day for three days.	**3 Days**	***F2***	***F5***	***MTHFR***
	Day 1	WT	HET	WT
		WT	HET	WT
	Day 2	WT	HET	WT
		WT	HET	WT
	Day 3	WT	HET	WT
		WT	HET	WT

Three operators at one site each analyzed the same sample in duplicate.	**3 Operators**	***F2***	***F5***	***MTHFR***
	Operator 1	WT	HET	HET
		WT	HET	HET
	Operator 2	WT	HET	HET
		WT	HET	HET
	Operator 3	WT	HET	HET
		WT	HET	HET

Study Description	Summary of Results			
One operator analyzed the same sample in duplicate using three lots of reagents.	**3 Reagent Lots**	***F2***	***F5***	***MTHFR***
	Lot 1 cartridge: 082107001A buffer: 082207001C	HET	WT	HET
		HET	WT	HET
	Lot 2 cartridge: 082707001C buffer: 050707001D	HET	WT	HET
		HET	WT	HET
	Lot 3 cartridge: 082807001A buffer: 082707001D	HET	WT	HET
		HET	WT	HET

Additional performance characteristics for Verigene *F5 / F2 / MTHFR* Nucleic Acid Tests:

Characteristic	Verigene *F5* Nucleic Acid Test	Verigene *F2* Nucleic Acid Test	Verigene *MTHFR* Nucleic Acid Test
Analytical sensitivity (LDL)	40 ng/µL	40 ng/µL	40 ng/µL
Call rate	98.3% (282 out of 287 calls made)	94.7% (272 out of 287 calls made)	93.4% (268 out of 287 calls made)
Diagnostic sensitivity	100% (95%CI =98.9 to 100%)	100% (95%CI =98.9 to 100%)	100% (95%CI =98.9 to 100%)
specificity	100% (95%CI =98.9 to 100%)	100% (95%CI =98.9 to 100%)	100% (95%CI =98.9 to 100%)
Precautions and warnings	In the *F5* gene, additional rare mutations other than the 1691G>A base change have been observed. Some of these mutations occur in regions covered by the oligonucleotide probes used in the test. The presence of one or more of these mutations may lead to an unknown result. NOTE: none of the mutations listed above have been linked to APC resistance. This test should not be used alone to diagnose thrombophilias. It is recommended that activated protein C (APC) testing be done alongside the genetic test.	In the *F2* gene, additional rare mutations other than the 20210G>A base change have been observed. Some of these mutations occur in regions covered by the oligonucleotide probes used in the test. The presence of one or more of these mutations may lead to an unknown result. This test should not be used alone to diagnose thrombophilias.	In the *MTHFR* gene, additional rare mutations other than the 677C>T base change have been observed. Some of these mutations occur in regions covered by the oligonucleotide probes used in the test. The presence of one or more of these mutations may lead to an unknown result. This test should not be used alone to diagnose thrombophilias.

Interferences	Performance not affected by • magnetic beads • heparin • hemoglobin Other possible interferences are not known.
Reagent stability	• The Test Cartridges are to be stored from 2°C to 8°C until the expiration date printed on the label. • The HC Sample Buffer is to be stored from 2°C to 8°C until the expiration date printed on the label. Neither the Test Cartridges nor the Sample Buffer can be frozen.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAR 24 2009

Nanosphere, Inc.
c/o Gregory W. Shipp, M.D.
Chief Medical Officer, VP of Medical and Regulatory Affairs and Quality Assurance
4088 Commercial Avenue
Northbrook, IL 60062

Re: k070597
Trade/Device Name: Verigene® F5 Nucleic Acid Test
Verigene® F2 Nucleic Acid Test
Verigene® MTHFR Nucleic Acid Test
Verigene® System
Regulation Number: 21 CFR 864.7280
21 CFR 862.2570
Regulation Name: Factor V Leiden DNA mutation detection systems
Instrumentation for clinical multiplex test systems
Regulatory Class: Class II
Product Code: NPQ, NPR, OMM, NSU
Dated: October 5, 2007
Received: October 9, 2007

Dear Dr. Gregory Shipp,

This letter corrects our substantially equivalent letter of October 11, 2007.

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 (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 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); 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.

This letter will allow you to continue marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0377. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). 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) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,

Maria M Chan

Maria M. Chan, Ph.D
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

2 a. Indications for use

510(k) Number (if known): **K070597**

Device Name: Verigene® System

Indications for Use: The Verigene System is a bench-top molecular diagnostics workstation that automates the analysis and detection of nucleic acids using gold nanoparticle probe technology.

Prescription Use ___X___ and/or Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (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 Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K070597

2 b. Indications for use

510(k) Number (if known): **K070597**

Device Name: Verigene *F5* Nucleic Acid Test

Indications for Use: The Verigene *F5* Nucleic Acid Test is indicated as an aid to diagnosis in the evaluation of patients with suspected thrombophilia.
The test is an *in vitro* diagnostic for the detection and genotyping of a single-point mutation (G to A at position 1691; also known as Factor V Leiden) of the human Factor V gene (*F5*; Coagulation Factor V gene), from isolated genomic DNA obtained from whole blood samples. The test is intended to be used on the Verigene System.

Prescription Use ___X___ and/or Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (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 Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K070597

2 c. Indications for use

510(k) Number (if known): **K070597**

Device Name: Verigene *F2* Nucleic Acid Test

Indications for Use: The Verigene *F2* Nucleic Acid Test is indicated as an aid to diagnosis in the evaluation of patients with suspected thrombophilia.

The test is an *in vitro* diagnostic for the detection and genotyping of a single-point mutation (G to A at position 20210) of the human Factor II gene (*F2*; prothrombin gene), from isolated genomic DNA obtained from whole blood samples. The test is intended to be used on the Verigene System.

Prescription Use ___X___ and/or Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (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 Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K070597

2 d. Indications for use

510(k) Number (if known): **K070597**

Device Name: Verigene *MTHFR* Nucleic Acid Test

Indications for Use: The Verigene *MTHFR* Nucleic Acid Test is indicated as an aid to diagnosis in the evaluation of patients with suspected thrombophilia and elevated levels of homocysteine or altered folate metabolism.

The test is an *in vitro* diagnostic for the detection and genotyping of a single-point mutation (C to T at position 677) of the human 5,10 methylenetetrahydrofolate reductase gene (*MTHFR*), from isolated genomic DNA obtained from whole blood samples. The test is intended to be used on the Verigene System.

Prescription Use ___X___ and/or Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (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 Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K070597