DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

February 26, 2015

SIEMENS HEALTHCARE DIAGNOSTICS, INC.
DONNA VELASQUEZ
REGULATORY TECHNICAL SPECIALIST
5210 PACIFIC CONCOURSE DRIVE
LOS ANGELES CA 90045

Re: K143373
Trade/Device Name: IMMULITE® 2000 Calcitonin Calibration Verification Material
IMMULITE® 2000 Prostatic Acid Phosphatase (PAP) Calibration Verification Material
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (assayed and unassayed)
Regulatory Class: I, Reserved
Product Code: JJX
Dated: December 1, 2014
Received: December 2, 2014

Dear Ms. Donna Velasquez:

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); 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 regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 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 Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -A

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMS No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143373

Device Name
IMMULITE® 2000 Calcitonin Calibration Verification Material

Indications for Use *(Describe)*
The IMMULITE® 2000 Calcitonin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Calcitonin assay on the IMMULITE 2000 systems.

Type of Use *(Select one or both, as applicable)*

X 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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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Dale: January 31, 2017
See *PRA Statement below.*

510(k) Number *(if known)*
K143373

Device Name
IMMULITE® 2000 Prostatic Acid Phosphatase (PAP) Calibration Verification Material

Indications for Use *(Describe)*
The IMMULITE® 2000 Prostatic Acid Phosphatase (PAP) Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE PAP assay on the IMMULITE 2000 systems.

Type of Use *(Select one or boll!,* as *applicable)*

X Prescription Use (Part 21 CFR 801 Subpart D) Over-The-Counter Use (21 CFR 801 Subpart C)

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510(k) Summary

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: K143373

1. **Submitter**

Mailing Address:	Siemens Healthcare Diagnostics Inc. 5210 Pacific Concourse Drive Los Angeles, CA 90045
Contact Person:	Donna Velasquez Regulatory Technical Specialist
Phone Number:	(310)-645-8200 x7403 (310)-
Fax Number:	645-9999
E-mail Address:	donna.velasquez@siemens.com
Date Prepared:	November 21, 2014

2. **Device Name**

Proprietary Name:	IMMULITE® 2000 Calcitonin Calibration Verification Material
Measurand:	Quality Control materials for IMMULITE® 2000 Calcitonin assay
Type of Test:	Calibration Verification Material (CVM) for IMMULITE® 2000 Calcitonin assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)

3. **Predicate Device Name**

IMMULITE® 2000 Intact PTH Calibration Verification Material (CVM)

Predicate 510(k) No: K140258

4. **Device Description:**

The IMMULITE® 2000 Calcitonin Calibration Verification Material (CVM) contains one set of four vials each 3mL after reconstitution. CVM1 contains bovine protein buffer matrix with preservatives and CVM2, CVM3, and CVM4 contain calcitonin in bovine protein buffer matrix with preservative.

5. **Intended Use:**

Indication for Use: See Indications for Use Statement below
The IMMULITE® 2000 Calcitonin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Calcitonin assay on the IMMULITE 2000 systems

Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	IMMULITE® 2000 Systems

6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:

A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 Calcitonin Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 Calcitonin CVM	**Predicate Device IMMULITE 2000 Intact PTH CVM**
Intended Use	The IMMULITE® Calcitonin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Calcitonin assay on the IMMULITE 2000 systems.	The IMMULITE® Intact PTH Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Intact PTH assay on the IMMULITE 2000 systems
Storage	:Ş-20°C	Same
Form	Lyophilized	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Matrix	Bovine protein buffer with preservatives	Same
Use	Single Use Only	Same

	DIFFERENCES	
	Candidate Device IMMULITE 2000 Beta-2 Microglobulin CVM	**Predicate Device IMMULITE 2000 Intact PTH CVM**
Analyte	Calcitonin	Intact PTH

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance Specifications for its intend use. The following tests were performed on the candidate device.

Stability Summary**:**

The stability study was conducted to validate real-time shelf life and open component (in-use or open vial) claim for the IMMULITE 2000 Calcitonin Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM. The Calibration Verification Materials are stable up to 5 years when stored at -20°C prior to opening.

Open Component stability studies presents results that support 8 hours of stability at ambient or room temperature (15-25°C) after reconstitution.

Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability calibrators/CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2,** and the dose value is determined from the reference calibrator curve.

Table 2: Stability Protocol Summary - LCLCVM Lot 005

CVM Level	Time-Points (Months)			
LCLCVM1	Day 0	48	54	60
LCLCVM2	Day 0	48	54	60
LCLCVM3	Day 0	48	54	60
LCLCVM4	Day 0	48	54	60

For Open Component testing, the results were determined from a 2-point adjustment. Using IMMULITE 2000 Calcitonin (L2KCL) kit lot 239, CVM lot 090 was tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions.

Stability Acceptance Criteria Summary:

The Acceptance Criteria for the Calcitonin Calibration Verification Material (CVM) require dose value of stability calibrators/CVM to fall between ±12% of assigned dose for CVM level 2 and ±10% for CVM levels 3 and 4 as shown in **Table 3**.

Table 3: Acceptance criteria for stability of IMMULITE 2000 Calcitonin CVM 005

CVM Level	**Assigned Dose (pg/mL)**	**Guideline Criteria % difference to assigned dose**	**Acceptable dose range (pg/mL)**
LCLCVM1	**0.00**	**N/A**	**:: 2.0**
LCLCVM2	**18.9**	**±12%**	**16.6 – 21.2**
LCLCVM3	**316**	**±10%**	**284 - 348**
LCLCVM4	**2082**	**±10%**	**1874 - 2290**

Traceability:

The IMMULITE Calcitonin CVMs are traceable to WHO 2nd IRP 89/620. The CVMs are manufactured using qualified materials and measurement procedures.

Value Assignment:

The IMMULITE Calcitonin CVMs are 4 level materials which are a subset of 7 level Calcitonin calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Calcitonin reagents and two point adjustors. The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The CVMs are manufactured using

qualified materials and measurement procedures. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples, spiked patient samples and controls using the assigned CVM values. Two levels of commercially available controls and 25 spiked normal patient samples were used to validate calibrator/CVM value assignments.

Expected Values/Target Values/Reference Range:
Each CVM level was tested for a total of 27 replicates; 9 runs and 3 replicates per run, 3 different reagent kit lots and 8 IMMULITE 2000 systems. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The target values are provided in the IMMULITE® 2000 CVM Calibration verification Material lot-specific value card. The expected assay range is 2 to 2000 pg/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Analyte Target Range Values

Analyte target levels	**CVM Level**	**Target Mean (ng/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (ng/mL)**	
	LCLCVM1	0.00	-	0.00	:S2.0
	LCLCVM2	18.9	2.95	13	24.8
	LCLCVM3	316	16	284	348
	LCLCVM4	2082	125	1832	2332
Assay Range	2 to 2000 pg/mL				

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 Calcitonin Calibration Verification Material is substantially equivalent to the predicate device intended for similar use. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 Calcitonin Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

SIEMENS

510(k) Summary

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: K143373

1. **Submitter**

Mailing Address:	Siemens Healthcare Diagnostics Inc. 5210 Pacific Concourse Drive Los Angeles, CA 90045
Contact Person:	Donna Velasquez Regulatory Technical Specialist
Phone Number:	(310) 645-8200 x7403 (310)
Fax Number:	645-9999
E-mail Address:	donna.velasquez@siemens.com
Date Prepared:	November 21, 2014

2. **Device Name**

Proprietary Name:	IMMULITE® 2000 Prostatic Acid Phosphatase (PAP)
Measurand:	Calibration Verification Material Quality Control materials for
Type of Test:	IMMULITE® 2000 PAP assay Calibration Verification Material (CVM) for IMMULITE® 2000 PAP assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)

3. **Predicate Device Name** — IMMULITE 2000 SHBG Calibration Verification Material (CVM)
Predicate 510(k) No: K140541

4. **Device Description:** The IMMULITE® 2000 Prostatic Acid Phosphatase (PAP) Calibration Verification Material (CVM) contains one set of four vials, 2mL each after reconstitution. CVM1 contains a bovine protein/buffer with 0.27% sodium azide and preservative. CVM2, CVM3, and CVM4 contain human prostatic acid phosphatase in a bovine protein/buffer matrix with 0.27% sodium azide and preservative.

5. **Intended Use:** See Indications for Use Statement below

Indication for Use: The IMMULITE® 2000 Prostatic Acid Phosphatase (PAP) Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE PAP assay on the IMMULITE 2000 systems.

Special Conditions for Use Statement(s): For prescription use only

Special Instrument Requirements: IMMULITE® 2000 Systems

6. Technological Characteristics and Substantial Equivalence Comparison with Predicate: A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 PAP Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 PAP CVM	**Predicate Device IMMULITE 2000 SHBG CVM**
Intended Use	The IMMULITE® Prostatic Acid Phosphatase (PAP) Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE PAP assay on the IMMULITE 2000 systems	The IMMULITE® SHBG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE SHBG assay on the IMMULITE 2000 systems
Form	Lyophilized	Same
Storage	2-8°C	Same
Levels	4	Same
Stability	Stable unopened until the expiration date	Same
Use	Single Use Only	Same

	DIFFERENCES	
	Candidate Device IMMULITE 2000 PAP CVM	**Predicate Device IMMULITE 2000 SHBG CVM**
Matrix	Bovine protein/buffer matrix with 0.27% Sodium Azide and preservatives	Buffered bovine/protein with preservatives
Analyte	PAP	SHBG

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intend use. The following tests were performed on the candidate device.

Stability Summary**:**

The stability study was conducted to validate real-time shelf life and open component (in-use or open vial) claim for the IMMULITE 2000 PAP Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM. The Calibration Verification Materials are stable up to 10 years when stored at 2-8°C prior to opening, and for 8 hours at ambient or room temperature (15-25°C) after opening.

Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

Table 2: Stability Protocol Summary – LPACVM Lot 005

CVM Level	Time-Points (Months)			
LCRPCVM1	Day 0	96	108	120
LCRPCVM2	Day 0	96	108	120
LCRPCVM3	Day 0	96	108	120
LCRPCVM4	Day 0	96	108	120

Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE PAP Calibration Verification Material (CVM) require dose value of stability CVMs to fall between ±20% of the assigned dose for CVM level 2 and 4 and ±15% of the assigned dose for CVM level 3 as shown in **Table 3**.

Table 3: Acceptance criteria for stability of IMMULITE 2000 PAP CVM Lot 005

CVM level	Assigned Dose (ng/mL)	Guideline Criteria % difference to assigned dose	Acceptable dose range (ng/mL)
LPACVM1	**0.00**	**N/A**	**::0.05**
LPACVM2	**1.3**	**±20%**	**1.04 – 1.56**
LPACVM3	**5.6**	**±15%**	**4.76 – 6.44**
LPACVM4	**140**	**±20%**	**112 – 168**

Traceability:

The IMMULITE PAP CVMs are traceable to an internal standard. The CVMs are manufactured using qualified materials and measurement procedures.

Value Assignment:

The IMMULITE PAP CVMs are 4 level materials which are a subset of 7 level PAP calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of PAP reagents and two point adjustors. The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. The CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples and controls using the assigned CVM values. The controls must fall within their target ranges. Six levels of commercially available controls and 27 samples (22 spiked serum samples and 5 normal female serum samples) were used to validate calibrator/CVM value assignments.

Expected Values/Target Values/Reference Range:

The CVMs are manufactured using qualified materials and measurement procedures. The PAP CVMs were tested on 15 replicates in total comprised of 5 runs and 3 replicates per run on 4 IMMULITE 2000 systems and 3 different reagent kit lots. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered

values for each run on each instrument independently. The CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples and controls using the assigned CVM values. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected assay range is 0.2 to 100 mg/L. The target values in **Table 4** can be considered as guidelines.

Table 4: Analyte Target Range Levels

Analyte target levels	CVM Level	Target Mean (ng/mL)	Standard Deviation (SD)	Guideline ±2SD Range (ng/mL)	
	LPACVM1	0.00	-	0.00	≤0.05
	LPACVM2	1.05	0.105	0.84	1.26
	LPACVM3	5.40	0.54	4.32	6.48
	LPACVM4 75% LCRPCVM4 + 25% LCRPCVM1	142 107	- 12.84	- 81.3	- 133
Assay Range	Up to 100 ng/mL				

NOTE: CVM4 requires dilution to ensure that the target value is within the +10% of the top of the reportable range of the assay.

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**

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

8. Conclusion:

The IMMULITE® 2000 PAP Calibration Verification Material is substantially equivalent to the predicate device intended for similar use. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 PAP Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.