DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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October 29, 2014

SIEMENS HEALTHCARE DIAGNOSTICS INC.
ASHA GARTLAND
TECHNICAL REGULATORY AFFAIRS SPECIALIST
511 BENEDICT AVENUE
TARRYTOWN NY 10591

Re: K142811
Trade/Device Name: Immulite® 2000 LH Calibration Verification Material (CVM),
Immulite® 2000 Free T3 Calibration Verification Material (CVM),
Immulite® 2000 Gastrin Calibration Verification Material (CVM)
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (assayed and unassayed)
Regulatory Class: I, reserved
Product Code: JJX
Dated: September 26, 2014
Received: September 29, 2014

Dear Ms. Asha Gartland:

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,

Courtney H. Lias -S

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

510(k) Number *(if known)*
K142811

Device Name
IMMULITE® 2000 LH Calibration Verification Material (CVM)
IMMULITE® 2000 Free T3 Calibration Verification Material (CVM)
IMMULITE® 2000 Gastrin Calibration Verification Material (CVM)

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

The IMMULITE® 2000 Free T3 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Free T3 assay on the IMMULITE 2000 systems

The IMMULITE® 2000 Gastrin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Gastrin assay on the IMMULITE 2000 systems

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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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: K142811

1. Submitter	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591
Contact Person:	Asha Gartland Technical Regulatory Affairs Specialist
Phone Number:	(914)-524-3257
Fax Number:	(914)-524-2101
E-mail Address:	asha.gartland@siemens.com
Date Prepared:	October 28th 2014
2. Device Name	
Proprietary Name:	**IMMULITE® 2000 LH Calibration Verification Material**
Measurand:	Quality Control materials for IMMULITE® 2000 LH assay Calibration Verification Material (CVM) for IMMULITE® 2000 LH assay
Type of Test:	
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 LH Calibration Verification Material (CVM) contains one set of four vials each 3.0mL after reconstitution. CVM1 contains lyophilized bovine serum with preservatives. CVM2, CVM3 and CVM4 contain various levels of LH antigen from human pituitary glands in a lyophilized bovine serum matrix with preservatives.

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5. <u>Intended Use</u>: **Indication for Use:**	See Indications for Use Statement below: The IMMULITE® 2000 LH Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE LH assay on the IMMULITE 2000 systems.
Special Conditions for Use Statement(s):	
Special Instrument Requirements:	For prescription use only IMMULITE® 2000 Systems
6. <u>Technological Characteristics and Substantial Equivalence</u> **Comparison with Predicate:**	A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 LH 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 LH CVM	**Predicate Device IMMULITE 2000 Intact PTH CVM**
Intended Use	The IMMULITE® 2000 LH Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE LH 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.
Form	Lyophilized	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Use	Single Use Only	Same

	DIFFERENCES	
	Candidate Device IMMULITE 2000 LH CVM	**Predicate Device IMMULITE 2000 Intact PTH CVM**
Analyte	LH	Intact PTH
Storage	2 -8 ^{o}C	≤-20°C
Matrix	Bovine serum with preservatives	Buffered bovine protein with preservatives

7. Non-Clinical Performance Testing

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

7.1 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 LH Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM before and after reconstitution.

The IMMULITE® 2000 LH Calibration Verification Materials are stable up to 9 years when stored at 2-8°C prior to opening and for 8 hours at ambient or room temperature (15-25°C) after reconstitution.

7.1.1 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 Time Points

CVM level	Time-Points (months)			
LLHCVM1	0	72	84	109
LLHCVM2	0	72	84	109
LLHCVM3	0	72	84	109
LLHCVM4	0	72	84	109

For Open Component testing, the results are determined from a 2-point adjustment. Using IMMULITE 2000 LH (L2KLH2) kit lot 305, LH CVM lot 090 was tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions and compared to the determinations at time zero.

7.1.2 Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE LH criteria requires dose value of stability calibrator/CVM to fall between ±18% of assigned dose for CVM level 2, ±12% for CVM level 3 and 14% for CVM level 4.

.The acceptance criterion is summarized in **Table 3**.

Table 3 Acceptance criteria for stability of IMMULITE 2000 LH CVM

CVM level	Assigned Dose (mIU/mL)	Guideline Criteria % difference to assigned dose	Acceptable dose range (mIU/mL)
LLHCVM1	0.00	Not Applicable	≤ 0.1
LLHCVM2	1.28	±18%	1.05 – 1.51
LLHCVM3	47.2	±12%	41.5 – 52.9
LLHCVM4	190	±14%	163 – 217

7.2 Traceability:

The IMMULITE LH is traceable to WHO 1st IRP 68/40 and 2nd IS 80/552. The CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:

IMMULITE 2000 LH CVMs are 4 level materials which are a subset of 13 level LH calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of LH reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using LH antigen stock and are traceable to WHO 1st IRP 68/40 and 2nd IS 80/552. Six levels of commercially available controls and 5 normal and 25 patient samples were used to validate calibrator/CVM value assignments.

The CVMs are manufactured using qualified materials and measurement procedures. The IMMULITE LH calibrators/CVMs were tested on 27 replicates in total, comprised of 9 runs, 3 replicates per run, 7 IMMULITE 2000 systems and 4 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. 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.

7.4 Expected Values/Reference Range:

Each CVM level was tested on tested on 27 replicates in total, comprised of 9 runs, 3 replicates per run, 7 IMMULITE 2000 systems and 4 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 CVM Calibration Verification Material lot-specific package insert.

The expected assay range is up to 200 mIU/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Target Values

Analyte target levels	**CVM Level**	***Target Mean (mIU/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (mIU/mL)**	
	LLHCVM1	0.00	-	0.00	≤0.1
	LLHCVM2	1.71	0.155	1.40	2.02
	LLHCVM3	51.5	3.1	45.3	57.7
	LLHCVM4	202	14.0	174	230
Assay Range	Up to 200 mIU/mL				

*Note: when CVMs are run by the customer, an actual value below and above the assay range will result when the customer programs the CVMs as calibration verifiers in the instrument software. If programmed as a patient or control, then the software will give values as < or > the assay lower and upper range.

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 LH Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 Intact PTH Calibration Verification Material. 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 LH 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: K142811

1. **Submitter**

Mailing Address: Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591

Contact Person: Asha Gartland
Technical Regulatory Affairs Specialist
Phone Number: (914)-524-3257
Fax Number: (914)-524-2101
E-mail Address: asha.gartland@siemens.com

Date Prepared: October 28th, 2014

2. **Device Name**

Proprietary Name: **IMMULITE® 2000 Free T3 Calibration Verification Material**
Measurand: Quality Control material for IMMULITE® 2000 Free T3 assay
Type of Test: Calibration Verification Material (CVM) for IMMULITE® 2000 Free T3 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**

Predicate 510(k) No: IMMULITE® 2000 HCG Calibration Verification Material (CVM) K133128

4. **Device Description:**

IMMULITE® 2000 Free T3 Calibration Verification Material (CVM) contains one set of four vials. CVM1 contains 4.0 mL processed lyophilized human serum with preservatives after reconstitution. CVM2, CVM3 and CVM4 contain 2.0mL/vial of various levels of 3,3[1] Triiodo-L-Thyronine (Free Acid) in processed lyophilized human serum with preservatives after reconstitution.

5. **Intended Use:**

Indication for Use: See Indications for Use Statement below
The IMMULITE® 2000 Free T3 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Free T3 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® Free T3 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 Free T3 CVM	**Predicate Device IMMULITE 2000 HCG CVM**
Intended Use	The IMMULITE® 2000 Free T3 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Free T3 assay on the IMMULITE 2000 systems	The IMMULITE® HCG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE HCG assay on the IMMULITE 2000 systems
Storage	≤-20°C	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Use	Single Use Only	Same
Matrix	Human serum with preservatives	Same

DIFFERENCES		
	Candidate Device Free T3 CVM	**Predicate Device IMMULITE 2000 HCG CVM**
Analyte	Free T3	HCG
Form	Lyophilized	Liquid

7. Non-Clinical Performance Testing

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

7.1 Stability Summary:

The stability study was conducted to validate shelf life claim for the IMMULITE 2000 Free T3 Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM before and after reconstitution.

The IMMULITE 2000 Free T3 Calibration Verification Materials are stable up to 1.5 years when stored at -20°C prior to reconstitution.

7.1.1 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 Time Points

CVM Level	**Time-Points (months)**			
LFT3CVM1	0	6	12	18
LFT3CVM2	0	6	12	18
LFT3CVM3	0	6	12	18
LFT3CVM4	0	6	12	18

7.1.2 Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE Free T3 criteria requires dose value of stability calibrator/CVM to fall between ±25% of assigned dose for CVM level 2, ±10% for CVM level 3 and 15% for CVM level 4.

The acceptance criterion is summarized in **Table 3**.

Table 3 Acceptance criteria for stability of IMMULITE 2000 Free T3 CVM

CVM level	Assigned Dose (pg/dL)	Guideline Criteria % difference to assigned dose	Acceptable dose range (pg/dL)
LFT3CVM1	**0.00**	**N/A**	**≤ 1.00**
LFT3CVM2	**1.48**	**±25%**	**1.11 – 1.85**
LFT3CVM3	**7.30**	**±10%**	**6.57 – 8.03**
LFT3CVM4	**44.5**	**±15%**	**37.8 – 51.2**

7.2 Traceability:
The IMMULITE 2000 Free T3 CVMs are traceable to an internal material which has been gravimetrically prepared. The CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:
The IMMULITE 2000 Free T3 CVMs are 4 level materials which are a subset of 6 level Free T3 calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Free T3 reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using Free T3 antigen stock and are traceable to an internal material which has been gravimetrically prepared. Six levels of commercially available controls and 30 normal patient samples were used to validate calibrator/CVM value assignments.

The calibrators/CVMs are manufactured using qualified materials and measurement procedures. The calibrators/CVMs were tested on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 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. 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. The controls must fall within their target ranges.

7.4 Expected Values/Reference Range:

Each CVM level was on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 4 IMMULITE 2000 systems and 3 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 Free T3 CVM Calibration Verification Material lot-specific package insert.*

The expected assay range is 1.0 to 40 pg/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Target Values

Analyte target levels	**CVM Level**	****Target Mean (pg/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (pg/mL)**	
	LF3CVM1	0.00	-	0.00	≤1.00
	LF3CVM2	1.48	0.185	1.11	1.85
	LF3CVM3	7.30	0.5475	6.21	8.40
	LF3CVM4*	44.5	-	-	-
	*90% LF3CVM4 + 10% LF3CVM1	40.1	3.00	34.1	46.1
Assay Range	1.0 to 40 pg/mL				

Note:

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

** When CVMs are run by the customer, an actual value below and above the assay range will result when the customer programs the CVMs as calibration verifiers in the instrument software. If programmed as a patient or control, then the software will give values as < or > the assay lower and upper range.

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 Free T3 Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 HCG Calibration Verification Material. 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 Free T3 Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

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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: K142811

1. **Submitter**

Mailing Address: Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591

Contact Person: Asha Gartland
Technical Regulatory Affairs Specialist
Phone Number: (914)-524-3257
Fax Number: (914)-524-2101
E-mail Address: asha.gartland@siemens.com

Date Prepared: October 28th, 2014

2. **Device Name**

Proprietary Name: **IMMULITE® 2000 Gastrin Calibration Verification Material**
Measurand: Quality Control materials for IMMULITE® 2000 Gastrin assay
Type of Test: Calibration Verification Material (CVM) for IMMULITE® 2000 Gastrin 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 DHEA-SO4 Calibration Verification Material (CVM)

Predicate 510(k) No: K140258

4. **Device Description:** The IMMULITE 2000 Gastrin Calibration Verification Material (CVM) contains one set of four vials, 2.0 mL each after reconstitution. CVM1 contains a lyophilized processed buffered human protein matrix with preservatives. CVM2, CVM3 and CVM4 contain various levels of synthetic-human gastrin in a lyophilized processed buffered human protein matrix with preservatives.

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

Indication for Use:	The IMMULITE® 2000 Gastrin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Gastrin 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 Gastrin 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 Gastrin CVM	**Predicate Device IMMULITE 2000 DHEA-SO4 CVM**
Intended Use	The IMMULITE® 2000 Gastrin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Gastrin assay on the IMMULITE 2000 systems	The IMMULITE® DHEA-SO4 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE DHEA-SO4 assay on the IMMULITE 2000 systems
Form	Lyophilized	Same
Levels	4	Same
Stability	Stable unopened until the expiration date	Same
Storage	≤-20°C	Same
Use	Single Use Only	Same

DIFFERENCES		
	Candidate Device IMMULITE 2000 Gastrin CVM	**Predicate Device IMMULITE 2000 DHEA-SO4 CVM**
Analyte	Gastrin	DHEA-SO4
Matrix	Buffered human protein with preservatives	Human serum with preservatives

7. Non-Clinical Performance Testing

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

7.1 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 Gastrin Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM, before and after reconstitution.
The IMMULITE 2000 Gastrin Calibration Verification Materials are stable up to 1.5 years when stored at ≤ -20°C prior to opening and for 8 hours at ambient or room temperature (15-25°C) after reconstitution.

7.1.1 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 Time Points

CVM Level	**Time-Points (Months)**			
LGACVM1	0	6	12	18
LGACVM2	0	6	12	18
LGACVM3	0	6	12	18
LGACVM4	0	6	12	18

For Open Component testing, the results are determined from a 2-point adjustment. Using IMMULITE 2000 Gastrin kit (L2KGA2) lot 229, CVM 090 was tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions.

7.1.2 Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE 2000 Gastrin criteria requires dose value of stability calibrator/CVMs to fall between ±12% of assigned dose for CVM level 2, ±8% for CVM level 3 and 12% for CVM level 4.

The acceptance criterion is summarized in **Table 3.**

Table 3: Acceptance criteria for stability of IMMULITE 2000 Gastrin CVM

CVM level	Assigned Dose (pg/mL)	Guideline Criteria % difference to assigned dose	Acceptable dose range (pg/mL)
LGACVM1	**0.00**	**N/A**	**≤ 10.0**
LGACVM2	**27.1**	**±12%**	**23.9 – 30.4**
LGACVM3	**409**	**±8%**	**376 – 442**
LGACVM4	**1244**	**±12%**	**1095 - 1393**

For Open Component stability testing the acceptance criteria are the same as guideline criteria described above and in **Table 3.**

7.2 Traceability:
The IMMULITE 2000 Gastrin CVMs are traceable to Medical Research Council Research Standard A for gastrin II, porcine (NIBSC 66/138). The CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:
The IMMULITE 2000 Gastrin CVMs are 4 level materials which are a subset of 10 level Gastrin calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Gastrin reagents and two point adjustors.
The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using Gastrin antigen stock and are traceable to Medical Research Council Research Standard A for gastrin II, porcine (NIBSC 66/138). Four levels of commercially available controls and 49 spiked serum samples and 5 normal serum samples were used to validate calibrator/CVM value assignments.

The CVMs are manufactured using qualified materials and measurement procedures. The CVMs were tested on 27 replicates in total, comprised of 9 runs, 3 replicates per run, 9 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. 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. The controls must fall within their target ranges.

7.4 Expected Values/Reference Range:

Each CVM level was tested tested on 27 replicates in total, comprised of 9 runs, 3 replicates per run, 9 IMMULITE 2000 systems and 3 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 Gastrin CVM Calibration Verification Material lot-specific package insert.*

The expected assay range is up to 1000 pg/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Target Values

Analyte target levels	**CVM Level**	****Target Mean (pg/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (pg/mL)**	
	LGACVM1	0.00	-	0.00	≤10
	LGACVM2	25.8	2.0	21.9	29.7
	LGACVM3	367	24	319	415
	LGACVM4*	1183	-	-	-
	*85% LGACVM4 + 15% LGACVM1	1006	80.5	845	1167
Assay Range	Up to 1000 pg/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

** When CVMs are run by the customer, an actual value below and above the assay range will result when the customer programs the CVMs as calibration verifiers in the instrument software. If programmed as a patient or control, then the software will give values as < or > the assay lower and upper range

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 Gastrin Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 DHEA-SO4 Calibration Verification Material 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 Gastrin Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.