

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k132739

B. Purpose for Submission:

New device

C. Measurand:

Calibration Verification Materials for IMMULITE® 2000 AFP, CA-15.3 and CA-125 assays

D. Type of Test:

Not applicable

E. Applicant:

Siemens Healthcare Diagnostics Inc.

F. Proprietary and Established Names:

IMMULITE® 2000 AFP Calibration Verification Material
IMMULITE® 2000 BR-MA Calibration Verification Material
IMMULITE® 2000 OM-MA Calibration Verification Material

G. Regulatory Information:

1. Regulation section:

21 CFR§862.1660 – Quality Control Material (assayed and unassayed)

2. Classification:

Class I, Reserved

3. Product code:

JJX, Single (Specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

IMMULITE® 2000 AFP Calibration Verification Material: The IMMULITE 2000 AFP Calibration Verification Material (CVM) is intended for monitoring system performance of the IMMULITE Immunoassay system for the quantitative measurement of AFP antigen.

IMMULITE® 2000 BR-MA Calibration Verification Material: The IMMULITE BR-MA Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration and reportable range of the IMMULITE BR-MA assay on the IMMULITE 2000 systems.

IMMULITE® 2000 OM-MA Calibration Verification Material: The IMMULITE OM-MA Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration and reportable range of the IMMULITE OM-MA assay on the IMMULITE 2000 systems.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For In Vitro Diagnostic Use
For Prescription use only

4. Special instrument requirements:

IMMULITE® 2000 Systems

I. Device Description:

IMMULITE 2000 AFP CVM: The CVM contains one set of four single-use vials, each containing 3mL of CVM. CVM1 contain bovine serum matrix with preservatives. CVM2, CVM3 and CVM4 contain low, intermediate and high levels of human source AFP respectively, in a bovine serum matrix with preservatives. The CVMs are supplied frozen in liquid form. In addition to using the CVM at their manufactured concentrations, alternate concentrations may be obtained by accurately diluting the assay-specific calibrator levels with each other.

IMMULITE 2000 BR-MA CVM: The CVM contains one set of four single-use vials, each containing 2 mL of CVM. CVM 1 contains a bovine serum matrix with preservatives. CVM2, CVM3, and CVM4 contain low, intermediate and high levels of human source CA 15-3 in a bovine serum matrix with preservatives. The CVMs are supplied frozen in liquid form. In addition to using the CVM at their manufactured concentrations, alternate concentrations may be obtained by accurately diluting the assay-specific calibrator levels with each other.

IMMULITE 2000 OM-MA CVM: The CVM contains one set of four single-use vials, each containing 2 mL of CVM. CVM 1 contains a bovine protein/buffer matrix with preservatives. CVM2, CVM3, and CVM4 contain low, intermediate and high levels of recombinant CA 125 in a bovine protein/buffer matrix with preservatives. CVMs are supplied in lyophilized form. In addition to using the CVM at their manufactured concentrations, alternate concentrations may be obtained by accurately diluting the assay-specific calibrator levels with each other.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) number(s):

IMMULITE/IMMULITE 1000 Third Generation PSA CVM, k122534
 Elecsys CA 15-3 II CalCheck 5, k122242
 Elecsys CA 125 II CalCheck 5, k102086

2. Comparison with predicate:

IMMULITE 2000 AFP CVM:

Similarities		
Item	Device IMMULITE 2000 AFP CVM	Predicate IMMULITE/IMMULITE 1000 Third Generation PSA CVM
Form	Liquid	Same
Stability	Stable until the expiration date when stored frozen	Same
Storage	-20°C	Same
Use	Single Use only	Same

Differences		
Item	Device IMMULITE 2000 AFP CVM	Predicate IMMULITE/IMMULITE 1000 Third Generation PSA CVM
Intended Use	The IMMULITE 2000 AFP Calibration Verification Material (CVM) is intended for monitoring system performance of the	The IMMULITE/IMMULITE 1000 Third Generation PSA Calibration Verification Material (CVM) is intended for monitoring

Differences		
Item	Device IMMULITE 2000 AFP CVM	Predicate IMMULITE/IMMULITE 1000 Third Generation PSA CVM
	IMMULITE Immunoassay system for the quantitative measurement of AFP antigen.	system performance of the IMMULITE Immunoassay system for the quantitative measurement of PSA antigen.
Analyte	AFP	PSA
Reagent Matrix	Bovine serum	Chicken Serum

IMMULITE 2000 BR-MA CVM:

Similarities		
Item	Device IMMULITE 2000 BR-MA CVM	Predicate Elecsys CA 15-3 II CalCheck 5
Intended Use	The IMMULITE BR-MA Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration and reportable range of the IMMULITE BR-MA assay on the IMMULITE 2000 systems.	The Elecsys CA 15-3 II CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the assay range established by the Elecsys CA 15-3 II reagent on the indicated Elecsys and cobas e immunoassay analyzers. For in vitro diagnostic use only.
Analyte	CA 15-3	Same

Differences		
Item	Device IMMULITE 2000 BR-MA CVM	Predicate Elecsys CA 15-3 II CalCheck 5
Form	Liquid	Lyophilized
Reagent Matrix	Bovine serum	Equine serum matrix (Level 1), Human serum matrix (Levels 2-5)
Stability	Stable until the expiration date when stored frozen	Stable until the expiration date when stored refrigerated.
Storage	-20°C	2-8°C
Use	Single Use only	Not For Single Use

IMMULITE 2000 OM-MA CVM:

Similarities		
Item	Device IMMULITE 2000 OM-MA CVM	Predicate Elecsys CA 125 II CalCheck 5
Intended Use	The IMMULITE OM-MA Calibration Verification Material	The Elecsys CA 125 II CalCheck 5 is an assayed control for use in

Similarities		
Item	Device IMMULITE 2000 OM-MA CVM	Predicate Elecsys CA 125 II CalCheck 5
	(CVM) is for in vitro diagnostic use in the verification of calibration and reportable range of the IMMULITE OM-MA assay on the IMMULITE 2000 systems.	calibration verification and for use in the verification of the assay range established by the Elecsys CA 125 II assay reagent on the indicated Elecsys and cobas e immunoassay analyzers. For in vitro diagnostic use only.
Analyte	CA 125	Same
Form	Lyophilized	Same
Stability	Stable until the expiration date when stored refrigerated	Same
Storage	2-8°C	Same
Differences		
Item	Device IMMULITE 2000 OM-MA CVM	Predicate Elecsys CA 125 II CalCheck 5
Reagent Matrix	Bovine serum	Level 1: Equine serum Levels 2-5: Human serum
Use	Single Use only	Not For Single Use

K. Standard/Guidance Document Referenced (if applicable):

CEN 13640: Stability Testing of In Vitro Diagnostic Reagents, 2002

Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material, 2005

Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators, 1999

L. Test Principle:

Not applicable

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Not applicable

b. *Linearity/assay reportable range:*

Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

i. Traceability:

IMMULITE 2000 AFP CVM: The IMMULITE AFP CVM is traceable to WHO 1st IS 72/225.

IMMULITE 2000 BR-MA CVM: The IMMULITE BR-MA CVMs are traceable to internally assigned reference calibrators prepared using BR-MA antigen stock solution (human-source CA 15-3). The reference calibrators are gravimetrically prepared from the source material.

IMMULITE 2000 OM-MA CVM: The IMMULITE OM-MA CVMs are traceable to internally assigned reference calibrators prepared using OM-MA antigen stock solution. The reference calibrators are gravimetrically prepared from the source material.

ii. Value Assignment:

The IMMULITE 2000 AFP CVMs, BR-MA CVMs and OM-MA CVMs are manufactured and value assigned using qualified materials and measurement procedures. Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. Value assignment is lot specific.

IMMULITE 2000 AFP CVM: Each CVM level was tested for 9 runs and 3 replicates per run for a total of 27 replicates. Three different reagent kit lots and 5 different instruments were used to gain 27 replicates. The CVMs dose values were generated using a curve generated by assigned reference calibrators. The analyte values were calculated based on the recovered values for each run on each instrument independently. CVM values were then averaged across all systems. 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 value card. The values in the table below can be considered as guidelines.

AFP CVM Level	Target Mean (IU/mL)	SD (IU/mL)	Guideline Range (IU/mL)	
CVM1	0.00	-	0.00	≤ 0.20
CVM2	3.03	0.225	2.58	3.48
CVM3	47.9	2.4	43.1	52.7
CVM4	413	-	-	-
(75% CVM4 + 25% CVM1)*	310	15.5	279	341

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

The expected assay range is 0.2 – 300 IU/mL.

IMMULITE 2000 BR-MA CVM: Each CVM level was tested for 9 runs and 3 replicates per run, a total of 27 replicates. Three different reagent kit lots and 6 different instruments were used to gain 27 replicates. The CVM values were calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. 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 value card. The values in the table below can be considered as guidelines.

BR-MA CVM Level	Target Mean (U/mL)	SD (U/mL)	Guideline Range (U/mL)	
CVM1	0.00	-	0.00	≤ 1.00
CVM2	18.8	1.4	16.0	21.6
CVM3	165	8.25	149	182
CVM4	291	14.5	262	320

The expected assay range is 1 – 300 U/mL.

IMMULITE 2000 OM-MA CVM: Each CVM level was tested for 9 runs and 3 replicates per run, a total of 27 replicates. Three different reagent kit lots and 9 different instruments were used to gain 27 replicates. 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. 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 value card. The values in the table below can be considered as guidelines.

OM-MA CVM Levels	Target Mean (U/mL)	SD	Guideline Range (U/mL)	
CVM1	0.00	-	0.00	≤ 2.00
CVM2	7.70	0.845	6.01	9.39
CVM3	57.0	2.85	51.3	62.7
CVM4	609	-	-	-
(85% of CVM4 + 15% of CVM1)*	518	28.5	461	575

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

The expected assay range is 2 – 500 U/mL.

iii. Stability:

The stability study was conducted to validate shelf life claim for the IMMULITE 2000 AFP CVM, IMMULITE 2000 BR-MA CVM and IMMULITE 2000 OM-MA CVM, to ensure that the CMVs maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM. The IMMULITE 2000 AFP CVMs are stable up to 3.5 years when stored frozen at -20°C prior to opening. The IMMULITE 2000 BR-MA CVMs are stable up to 4.5 years when stored frozen at -20°C prior to opening. The IMMULITE 2000 OM-MA CVMs are stable up to 9 years when stored refrigerated at 2-8°C prior to opening.

iv. Matrix effect:

The Matrix Effects Studies were performed to describe any significant difference between the IMMULITE 2000 AFP CVM, IMMULITE 2000 BR-MA CVM and IMMULITE 2000 OM-MA CVM and typical patient samples in terms of conditions known to cause analytical error.

IMMULITE 2000 AFP CVM: A stock solution of AFP antigen was used to prepare the spiking solutions for studying matrix effects. Three spiking solutions were prepared from stock solution. Each spiking solution was spiked into matrix (Bovine Serum) and patient sample (1 part spiking solution to 19 parts matrix or sample) to generate three sets of spiked samples (concentrations at 9.91 IU/mL, 29.76 IU/mL and 67.81 IU/mL).

IMMULITE 2000 BR-MA CVM: A stock solution of BR-MA antigen (CA15.3) was used to prepare the spiking solutions for studying matrix effects. Three spiking solutions were prepared from stock solution. Each spiking solution was spiked into matrix (Bovine Serum) and patient sample (1 part spiking solution to 19 parts matrix or sample) to generate three sets of

spiked samples (concentrations at 282 U/mL, 617 U/mL and 1,168 U/mL).

IMMULITE 2000 OM-MA CVM: A stock solution of OM-MA antigen (CA125) was used to prepare the spiking solutions for studying matrix effects. Three spiking solutions were prepared from stock solution. Each spiking solution was spiked into Bovine protein/buffer matrix and patient sample (1 part spiking solution to 19 parts matrix or sample) to generate three sets of spiked samples (concentrations at 627 U/mL, 1,207 U/mL and 2,408 U/mL).

The spiked AFP, BR-MA and OM-MA samples were run in their respective assays on IMMULITE 2000 platform. The % recovery of antigen in the spiked matrix was compared to the % recovery in the spiked patient sample. Each of the tested samples met the acceptance criteria: the grand mean of the recoveries must be within $100\% \pm 10\%$ of the expected value with no mean recovery being more than $100\% \pm 15\%$.

d. Detection limit:

Not applicable

e. Analytical specificity:

Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

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

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.