SIEMENS

CE 0197

ADVIA Centaur® CP
Immunoassay System

CKMB

Assay Summary

Sample Type	***Serum, Heparinized Plasma***
Sample Volume	***100 µL***
Calibrator	***CKMB***
Sensitivity and Assay Range	***0.18 – 300 ng/mL (0.0023 – 3.75 nmol/L)***

Contents

REF	*Contents*	*Number of Tests*
07516647 (110774)	5 ReadyPack® primary reagent packs containing ADVIA Centaur® CKMB Lite Reagent and Solid Phase ADVIA Centaur and ADVIA Centaur CP CKMB Master Curve cards	500
or		
00481201 (110773)	1 ReadyPack primary reagent pack containing ADVIA Centaur CKMB Lite Reagent and Solid Phase ADVIA Centaur and ADVIA Centaur CP CKMB Master Curve cards	100

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Intended Use

For *in vitro* diagnostic use in the quantitative determination of CK-MB in serum or heparinized plasma using the ADVIA Centaur® CP System.

Materials Required But Not Provided

REF	*Description*	*Contents*
09318028 (672174)	CKMB Calibrator	2 vials of low calibrator CAL L 2 vials of high calibrator CAL H

Optional Reagents

REF	*Description*	*Contents*
04542396 (110323)	ADVIA Centaur CKMB Diluent DIL	2 ReadyPack ancillary reagent packs containing 5 mL/pack
07867768 (105805)	CKMB Master Curve Material	10 x 2 mL

Summary and Explanation of the Test

The enzyme creatine kinase (CK) is a dimer composed of either two B monomers (CK-BB), two M monomers (CK-MM), or the MB hybrid (CK-MB). The isoenzymes have the same molecular weight and catalyze the same reaction, but differ in molecular structure and in their source. CK-MM is found primarily in skeletal muscle and CK-BB originates in the brain tissue and intestinal tract, while the primary source of CK-MB is the myocardium.[1,2]

The quantitation of CK-MB levels is used as an aid in the diagnosis of myocardial injury.[3,4] Elevated CK-MB levels are associated with myocardial cell death and damage due to acute myocardial infarction (AMI).[4] CK-MB levels can be detected as a result of myocardial injury within 3 to 8 hours following the onset of chest pain with peak concentrations being achieved within 12 to 24 hours and usually returning to baseline levels within 24 to 48 hours.[5] CK-MB samples analyzed at the appropriate time intervals can detect this typical rise and fall pattern, which is indicative of myocardial cell damage. Some myocardial infarctions are relatively minor and produce very low quantities of CK-MB. Therefore, it is important to have a sensitive assay that can detect these minor increases in CK-MB levels.

Conditions other than myocardial infarction, especially cardiac surgery[6,7] for coronary bypass, valve replacement, or repair of congenital defects, may cause elevated serum CK-MB levels.[3] However, in these cases, the CK-MB levels do not exhibit the characteristic rise and fall pattern indicative of myocardial infarction.[1] The CK-MB levels of such patients are sometimes monitored to detect myocardial infarction as a complication.[8]

Other conditions may cause elevated CK-MB levels and should be considered when the diagnosis of myocardial infarction is unclear. These conditions include skeletal muscle trauma,[9] dermatomyositis,[10] Duchenne's muscular dystrophy,[11] Reye's syndrome, rhabdomyolysis, drug overdoses, delirium tremens, or chronic alcohol poisoning.

Assay Principle

The ADVIA Centaur CP CKMB assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of two antibodies. The first antibody, in the Lite Reagent, is a monoclonal mouse anti-CK-MB antibody labeled with acridinium ester. The second antibody, in the Solid Phase, is a monoclonal mouse anti-CK-BB antibody, which is covalently coupled to paramagnetic particles.

The system automatically performs the following steps:

- dispenses 100 µL of sample into a cuvette
- dispenses 50 µL of Lite Reagent and incubates for 6.3 minutes at 37°C
- dispenses 225 µL of Solid Phase and incubates for 3.0 minutes at 37°C
- separates, aspirates, and washes the cuvettes with Wash 1
- dispenses 300 µL each of Acid Reagent (R1) and Base Reagent (R2) to initiate the chemiluminescent reaction
- reports results according to the selected option, as described in the system operating instructions or in the online help system

A direct relationship exists between the CK-MB in a sample and the relative light units (RLUs) detected by the system. The ADVIA Centaur CP CKMB assay measures the immunological activity of CK-MB and reports the concentration in common units (ng/mL) or SI units (nmol/L).

Specimen Collection and Handling

Serum or heparinized plasma are the recommended sample types for this assay.

Evaluation of heparinized plasma samples may result in up to a +12.5% bias. It is not recommended that heparinized plasma and serum samples from the same patient be used interchangeably with this assay.

The following recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS):[12]

- Collect all blood samples observing universal precautions for venipuncture.
- Allow samples to clot adequately before centrifugation.
- Keep tubes stoppered and upright at all times.
- Do not use samples that have been stored at room temperature for longer than 4 hours.
- Tightly cap and refrigerate specimens at 2 to 8°C if the assay is not completed within 4 hours.
- Freeze samples at or below -20°C if the sample is not assayed within 48 hours.
- Freeze samples only once and mix thoroughly after thawing.

Before placing samples on the system ensure that:

- Samples are free of fibrin or other particulate matter.
- Samples are free of bubbles.

Reagents

Store the reagents upright at 2–8°C.
Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to the *Operator's Guide*.

Reagent Pack	Reagent	Volume	Ingredients	Storage	Stability
ADVIA Centaur CKMB ReadyPack primary reagent pack	Lite Reagent	5.0 mL/ reagent pack	monoclonal mouse anti-CK-MB antibody (~0.11 µg/mL) labeled with acridinium ester in buffer with sodium azide (0.11%), protein stabilizers, and preservatives	2–8°C	until the expiration date on the pack label. For onboard stability, refer to *Onboard Stability and Calibration Interval.*
	Solid Phase	22.5 mL/ reagent pack	monoclonal mouse anti-CK-BB antibody (~0.06 mg/mL) covalently coupled to paramagnetic particles in buffer with protein stabilizers, sodium azide (0.1%), and preservatives	2–8°C	until the expiration date on the pack label. For onboard stability, refer to *Onboard Stability and Calibration Interval.*
ADVIA Centaur CKMB DIL ReadyPack ancillary reagent pack	CKMB Diluent	5.0 mL/ reagent pack	equine serum with sodium azide (< 0.1%) and preservatives	2–8°C	until the expiration date on the pack label or 28 consecutive days after accessing the ancillary reagent pack

Safety data sheets (MSDS/SDS) available on siemens-healthineers.com.

The summary of safety and performance for this *in vitro* diagnostic medical device is available to the public in the European Database on Medical Devices (EUDAMED) when this database is available and the information has been uploaded by the Notified Body. The web address of the EUDAMED public website is: https://ec.europa.eu/tools/eudamed.

NOTE: Sodium azide can react with copper and lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent the buildup of azides, if disposal into a drain is in compliance with federal, state, and local requirements.

CAUTION: This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

For Professional Use.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For *In Vitro* Diagnostic Use.

Loading Reagents

Ensure that the system has sufficient primary and ancillary reagent packs. For detailed information about preparing the system, refer to the system operating instructions or to the online help system.

Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to the *Operator's Guide*.

Load the primary reagent packs in the primary reagent area. The arrows on the end label can be used as a placement guide. However left, center, and right placement of the primary reagent packs is not required because there is only one reagent probe on the ADVIA Centaur CP System. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about loading reagents, refer to the system operating instructions or to the online help system.

If automatic dilution of a sample is required, load ADVIA Centaur CKMB Diluent in the ancillary reagent area.

Onboard Stability and Calibration Interval

Onboard Stability	Calibration Interval
28 days	28 days

Additionally, the ADVIA Centaur CP CKMB assay requires a two-point calibration:

- when changing lot numbers of primary reagent packs
- when replacing system components
- when quality control results are repeatedly out of range

NOTE:

- Discard the primary reagent packs at the end of the onboard stability interval.
- Do not use reagents beyond the expiration date.

Master Curve Calibration

The ADVIA Centaur CP CKMB assay requires a Master Curve calibration when using a new lot number of Lite Reagent and Solid Phase. For each new lot number of Lite Reagent and Solid Phase, use the barcode reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions or to the online help system.

Performing Quality Control

To monitor system performance and chart trends, as a minimum requirement, two levels of quality control material should be assayed on each day that samples are analyzed. Quality control samples should also be assayed when performing a two-point calibration. Treat all quality control samples the same as patient samples.

Siemens Healthcare Diagnostics recommends the use of commercially available quality control materials with at least 2 levels (low and high). For assistance in identifying a quality control material, refer to *ADVIA Centaur Quality Control Material Supplement* available on siemens-healthineers.com.

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

• Following a valid calibration

• With use of a new lot of reagent

• When troubleshooting test results that do not match clinical conditions or symptoms

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the system online help.

If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.

Sample Volume

This assay requires 100 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For detailed information about determining the minimum required volume, refer to the system operating instructions or to the online help system.

Assay Procedure

For detailed procedural information, refer to the system operating instructions or to the online help system.

Procedural Notes

Calculations

For detailed information about how the system calculates results, refer to the system operating instructions or to the online help system.

The system reports serum CK-MB results in ng/mL (common units) or nmol/L (SI Units), depending on the units defined when setting up the assay. The conversion formula is 1 ng/mL = 0.0125 nmol/L.

Dilutions

- Serum samples with CK-MB levels greater than 300 ng/mL (3.75 nmol/L) must be diluted and retested to obtain accurate results.
- Patient samples can be automatically diluted by the system.
- For automatic dilutions, ensure that ADVIA Centaur CKMB Diluent is loaded and set the system parameters as follows:

  Dilution point: ≤ 300 ng/mL (3.75 nmol/L)

  Dilution factor: 2, 10

  For detailed information about automatic dilutions, refer to the system operating instructions or to the online help system.

High Dose Hook Effect

Patient samples with high CK-MB levels can cause a paradoxical decrease in the RLUs (high dose hook effect). In this assay, patient samples with CK-MB levels as high as 500 ng/mL (6.25 nmol/L) will assay greater than 300 ng/mL (3.75 nmol/L).

Disposal

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner, and in compliance with all federal, state, and local requirements.

Limitations

Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[13] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.

Serum specimens that are . . .	*Demonstrate ≤ 5% change in results up to . . .*
hemolyzed	150 mg/dL of hemoglobin
lipemic	1000 mg/dL of triglycerides
icteric	40 mg/dL of bilirubin

Interference testing was determined according to CLSI Document EP7-A2.[14]

Expected Results

The expected results for the ACS:180® CKMB II assay were previously established using serum samples. CK-MB results from 233 apparently healthy individuals gave a median result of 0.78 ng/mL (0.0098 nmol/L).

Serum CK-MB results from 167 hospitalized patients with noncardiac related disorders gave a median result of 1.49 ng/mL (0.0186 nmol/L).

Serum CK-MB results from 42 patients with confirmed myocardial injury ranged up to 144 ng/mL (1.80 nmol/L), with a median result of 25.4 ng/mL (0.3175 nmol/L).

This data was analyzed using Cumulative Distribution analysis, which indicated a CK-MB value of > 5.0 ng/mL (0.0625 nmol/L) is highly suggestive of myocardial infarction. However, using the Relative Index (RI) in addition to the actual CK-MB level can help in differentiating elevated CK-MB from noncardiac and cardiac tissue sources (refer to *Interpretation of Results*).

These results were confimed for the ADVIA Centaur CP CKMB assay by analyzing 255 serum samples in the range of 0.23 to 205.19 ng/mL (0.00 to 2.57 nmol/L). Refer to *Method Comparison.*

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.[15]

Interpretation of Results

Serial sampling at the appropriate time intervals will result in the typical rise and fall pattern of CK-MB levels in patients experiencing myocardial infarction. Elevated CK-MB levels may be related to non-AMI events such as congestive heart failure, strenuous exercise, or trauma. These events should be considered when interpreting CK-MB results. The use of the ratio of CK-MB concentration to total CK concentration can assist in differentiating cardiac and noncardiac sources and is defined as follows:

$$RI = \frac{\text{ADVIA Centaur CP CKMB (ng/mL)}}{\text{Total CK Activity (U/L)}} \times 100$$

RI is analogous to the % CK-MB calculation obtained by electrophoresis.

Due to differences in testing apparatus for total CK, location, and patient populations, each laboratory should establish its own reference range(s) for the diagnostic evaluation of patient results.

Performance Characteristics

Specificity

The cross-reactivity of the assay with CK-MM and CK-BB was determined by adding these isoenzymes to samples containing CK-MB. The CK-MB level in the samples was then determined.

	CK-MB value without cross-reactant		*CK-MB value with cross-reactant*	
Cross-reactant	***(ng/mL)***	***(nmol/L)***	***(ng/mL)***	***(nmol/L)***
CK-MM; 5000 ng/mL	3.82	0.048	3.86	0.048
	4.32	0.054	4.33	0.054
	3.26	0.041	3.34	0.042
	3.34	0.042	3.43	0.043

Cross-reactant	CK-MB value without cross-reactant (ng/mL)	(nmol/L)	CK-MB value with cross-reactant (ng/mL)	(nmol/L)
	3.76	0.047	3.86	0.048
CK-BB; 1000 ng/mL	3.86	0.048	3.84	0.048
	4.28	0.054	4.27	0.053
	3.30	0.041	3.24	0.041
	3.37	0.042	3.31	0.041
	3.81	0.048	3.79	0.047

Interference testing was previously determined for the ACS:180 CKMB II assay.

Sensitivity and Assay Range

The ADVIA Centaur CP CKMB assay measures CK-MB concentrations up to 300 ng/mL (3.75 nmol/L) with a minimum detectable concentration (analytical sensitivity) of 0.18 ng/mL (0.0023 nmol/L). Analytical sensitivity is defined as the concentration of CK-MB that corresponds to the RLUs that are two standard deviations greater than the mean RLUs of 20 replicate determinations of the CK-MB zero standard.

Method Comparison

For 255 samples in the range of 0.23 to 205.19 ng/mL (0.00 to 2.57 nmol/L), the relationship between the ADVIA Centaur CP CKMB assay and the ACS:180 CKMB II assay is described by the equation:

ADVIA Centaur CP CKMB = 1.07 (ACS:180 CKMB II) – 0.3 ng/mL

Correlation coefficient (r) = 0.99

For 257 samples in the range of 0.31 to 231.28 ng/mL (0.00 to 2.89 nmol/L), the relationship between the ADVIA Centaur CP CKMB assay and the ADVIA Centaur CKMB assay is described by the equation:

ADVIA Centaur CP CKMB = 1.02 (ADVIA Centaur CKMB) – 0.7 ng/mL

Correlation coefficient (r) = 0.99

Dilution Recovery

Four human serum samples in the range of 58.3 to 208.3 ng/mL (0.73 to 2.60 nmol/L) of CK-MB were diluted 1:2, 1:4, 1:8, and 1:16 with CKMB Diluent and assayed for recovery and parallelism. The recoveries ranged from 88.0% to 112.9% with a mean of 99.0%.

Sample	Dilution	Observed (ng/mL)	Expected (ng/mL)	Observed (nmol/L)	Expected (nmol/L)	Recovery %
1	—	58.28		0.73		
	1:2	29.24	29.14	0.37	0.36	100.4
	1:4	14.55	14.57	0.18	0.18	99.8
	1:8	7.86	7.28	0.10	0.09	107.9
	1:16	4.11	3.64	0.05	0.05	112.9
	Mean					105.3
2	—	208.25		2.60		
	1:2	93.34	104.13	1.17	1.30	89.6
	1:4	45.81	52.06	0.57	0.65	88.0
	1:8	24.81	26.03	0.31	0.33	95.3
	1:16	13.23	13.02	0.17	0.16	101.6
	Mean					93.6
3	—	108.24		1.35		
	1:2	50.61	54.12	0.63	0.68	93.5
	1:4	26.87	27.06	0.34	0.34	99.3

Sample	Dilution	Observed (ng/mL)	Expected (ng/mL)	Observed (nmol/L)	Expected (nmol/L)	Recovery %
	1:8	13.82	13.53	0.17	0.17	102.1
	1:16	7.44	6.76	0.09	0.08	110.0
	Mean					101.2
4	—	205.64		2.57		
	1:2	92.90	102.82	1.16	1.29	90.4
	1:4	48.05	51.41	0.60	0.64	93.5
	1:8	24.65	25.70	0.31	0.32	95.9
	1:16	13.32	12.85	0.17	0.16	103.6
	Mean					95.8
Mean						**99.0**

Spiking Recovery

Varying amounts of CK-MB were added to six samples with endogenous CK-MB levels of 6.84 to 10.42 ng/mL (0.0855 to 0.1303 nmol/L). The recoveries ranged from 89.5% to 111.4% with a mean of 103.1%.

Sample	Amount Added (ng/mL)	Observed (ng/mL)	Amount Added (nmol/L)	Observed (nmol/L)	Recovery %
1	—	7.60	—	0.0950	
	10.22	16.81	0.1278	0.2101	90.1
	43.53	54.21	0.5441	0.6776	107.1
	107.50	126.26	1.3438	1.5783	110.4
	214.74	246.91	2.6843	3.0864	111.4
	471.22	514.93	5.8903	6.4366	107.7
	Mean				105.3
2	—	7.81	—	0.0976	
	10.22	17.79	0.1278	0.2224	97.7
	43.53	52.08	0.5441	0.6510	101.7
	107.50	123.35	1.3438	1.5419	107.5
	214.74	236.84	2.6843	2.9605	106.7
	471.22	480.89	5.8903	6.0111	100.4
	Mean				102.8
3	—	6.95	—	0.0869	
	10.22	16.77	0.1278	0.2096	96.1
	43.53	52.63	0.5441	0.6579	104.9
	107.50	121.54	1.3438	1.5193	106.6
	214.74	235.90	2.6843	2.9488	106.6
	471.22	502.53	5.8903	6.2816	105.2
	Mean				103.9
4	—	7.85	—	0.0981	
	10.82	18.25	0.1353	0.2281	96.1
	44.66	54.33	0.5583	0.6791	104.1
	114.43	127.25	1.4304	1.5906	104.3
	225.98	245.80	2.8248	3.0725	105.3
	507.26	517.33	6.3408	6.4666	100.4
	Mean				102.1
5	—	10.42	—	0.1303	
	10.82	22.18	0.1353	0.2773	108.7
	44.66	58.17	0.5583	0.7271	106.9
	114.43	131.28	1.4304	1.6410	105.6
	225.98	258.44	2.8248	3.2305	109.8

Sample	Amount Added (ng/mL)	Observed (ng/mL)	Amount Added (nmol/L)	Observed (nmol/L)	Recovery %
	507.26	531.94	6.3408	6.6493	102.8
	Mean				106.8
6	—	6.84	—	0.0855	
	10.82	16.52	0.1353	0.2065	89.5
	44.66	50.91	0.5583	0.6364	98.7
	114.43	120.90	1.4304	1.5113	99.7
	225.98	237.05	2.8248	2.9631	101.9
	507.26	509.22	6.3408	6.3653	99.0
	Mean				97.8
Mean					**103.1**

Spiking recovery testing was previously determined for the ADVIA Centaur CKMB Assay.

Precision

Precision was evaluated according to the CLSI protocol EP5-A2.[16] According to this protocol, the assay was run 2 times per day, for 10 days, using 1 reagent lot, on 3 instruments. The instrument was calibrated on the first run of day one. Assay results were calculated using the two-point calibration. The following results were obtained:

Mean (ng/mL)	Mean (nmol/L)	Within-run CV(%)	Between run CV(%)	Total CV(%)
3.12	0.04	2.68	3.92	4.74
29.22	0.37	2.41	3.50	4.25
91.22	1.14	3.14	4.90	5.82

Based on internal testing on the ADVIA Centaur CP system, the overall reproducibility is estimated to be ≤ 7% CV for samples tested and includes multiple reagent lots, instruments, days, and replicates. Performance of the assay at individual laboratories may vary.

Traceability of Standardization

The ADVIA Centaur CP CKMB assay is traceable to an internal standard manufactured using highly purified material. Assigned values for calibrators are traceable to this standardization.

Technical Assistance

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or patient is established.

For customer support, contact your local technical support provider or distributor.

siemens-healthineers.com

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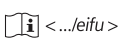
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Manufacturer	5.1.1[a]		Authorized representative in the European Community	5.1.2[a]
	Use-by date	5.1.4[a]		Authorized representative in Switzerland	Proprietary
	Catalog number	5.1.6[a]		Batch code	5.1.5[a]
	Consult Instructions for Use	5.4.3[a]		Contains sufficient for <n> tests	5.5.5[a]
	Internet URL address to access the electronic instructions for use	Proprietary		Version of Instructions for Use	Proprietary
	*In vitro* diagnostic medical device	5.5.1[a]		Revision	Proprietary
RxOnly	Prescription device (US only)	FDA[c]		Unique Device Identifier	5.7.10[b]
	CE Marking with Notified Body	EU IVDR[d]		CE Marking	EU IVDR[d]
	Temperature limit	5.3.7[a]		Keep away from sunlight	5.3.2[a]
	Upper limit of temperature	5.3.6[a]		Lower limit of temperature	5.3.5[a]
	Do not re-use	5.4.2[a]		Do not freeze	Proprietary
	Recycle	1135[e]		This way up	0623[e]
	Biological risks	5.4.1[a]		Caution	5.4.4[a]
	Common Units	Proprietary		Document face up[f]	1952[e]
YYYY-MM-DD	Date format (year-month-day)	N/A		International System of Units	Proprietary
	Target	Proprietary	**YYYY-MM**	Date format (year-month)	N/A
				Interval	Proprietary

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Handheld barcode scanner	Proprietary	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	Proprietary
LOT DTL	Lot details	Proprietary	MC DEF	Master Curve definition	Proprietary
CAL LOT VAL	Calibrator lot value	Proprietary	CONTROL LOT VAL	Quality control lot value	Proprietary

[a] International Standard Organization (ISO). ISO 15223-1 Medical Devices- Symbols to be used with medical device labels, labelling and information to be supplied.

[b] ISO 15223-1:2020-04

[c] Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.

[d] IVDR REGULATION (EU) 2017/746

[e] International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.

[f] Indicates Assay-*e*Note

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