

CKMB

Current revision and date ^a	Rev. M, 2015-01	
Product Name	ADVIA Centaur® CKMB assay (500 test)	REF 07516647 (110774)
	ADVIA Centaur CKMB assay (100 test)	REF 00481201 (110773)
Systems	ADVIA Centaur system ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur CKMB Calibrator (6 pack)	REF 02946856 (672179)
	ADVIA Centaur CKMB Calibrator (2 pack)	REF 09318028 (672174)
Specimen Types	Serum, Heparinized Plasma	
Assay Range	0.18–300 ng/mL (0.0023–3.75 nmol/L)	
Reagent Storage	2–8°C	
Reagent On-System Stability	28 days	

^a In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

For *in vitro* diagnostic use in the quantitative determination of CK-MB in serum or heparinized plasma using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems.

Summary and Explanation

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 in serum 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 3–8 hours following the onset of chest pain with peak concentrations being achieved within 12–24 hours and usually returning to baseline levels within 24–48 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.

Principles of the Procedure

The ADVIA Centaur 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.

Reagents

Reagent	Description	Storage	Reagent 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	Unopened: Stable until the expiration date on the carton On-system: 28 days
ADVIA Centaur CKMB ReadyPack primary reagent pack; Solid Phase Reagent	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	Unopened: Stable until the expiration date on the carton On-system: 28 days
ADVIA Centaur CKMB ReadyPack ancillary reagent pack; CKMB Diluent ^a 	5.0 mL/reagent pack equine serum with sodium azide (< 0.1%) and preservatives	2–8°C	Unopened: Stable until the expiration date on the pack On-system: 28 days
ADVIA Centaur CKMB Diluent ^a 	10.0 mL/vial equine serum with sodium azide (< 0.1%) and preservatives	2–8°C	Unopened: Stable until the expiration date on the vial

^a See *Optional Materials*

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on www.siemens.com/diagnostics.



CAUTION

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

Contains sodium azide as a preservative. Sodium can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

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 prevailing regulatory requirements.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.



CAUTION

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, see the system operating instructions.



CAUTION

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

Storing and Stability

Store the reagents upright at 2–8°C.

Protect reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from heat and light sources.

All reagents are stable at 2–8°C until the expiration date on the packaging.

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 +20% 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):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 2–8°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.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Procedure

Materials Provided

The following materials are provided:

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

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description
REF 02946856 (672179)	ADVIA Centaur CKMB Calibrator 6 vials of low calibrator <input type="checkbox"/> CAL <input type="checkbox"/> L 6 vials of high calibrator <input type="checkbox"/> CAL <input type="checkbox"/> H
REF 09318028 (672174)	ADVIA Centaur CKMB Calibrator 2 vials of low calibrator <input type="checkbox"/> CAL <input type="checkbox"/> L 2 vials of high calibrator <input type="checkbox"/> CAL <input type="checkbox"/> H

Optional Materials

The following materials may be used to perform this assay, but are not provided:

Item	Description
REF 04542396 (110323)	ADVIA Centaur CKMB Diluent <input type="checkbox"/> DIL 2 ReadyPack ancillary reagent packs containing 5 mL/pack
REF 02116411 (672230)	ADVIA Centaur CKMB Diluent <input type="checkbox"/> DIL 10 mL/vial
REF 105805	ADVIA Centaur CKMB Master Curve Material 10 x 2 mL

Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following steps:

1. Dispenses 100 µL of sample into a cuvette.
2. Dispenses 50 µL of Lite Reagent and incubates for 5.0 minutes at 37°C.
3. Dispenses 225 µL of Solid Phase and incubates for 2.5 minutes at 37°C.
4. Separates, aspirates, and washes the cuvettes with reagent water.

Note For information about reagent water, refer to the system operating instructions.

5. Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
6. Reports results according to the selected option, as described in the system operating instructions.

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

Preparing the System

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

Load the ReadyPack reagent packs in the primary reagent area using the arrows as a placement guide. 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.

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

Preparing the Samples

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, see the system operating instructions.

Before placing samples on the system, ensure that samples have the following characteristics:

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

On-System Stability

The ADVIA Centaur CKMB assay reagents are stable unopened until the expiration date on the carton or onboard the system for 28 days.

Performing Calibration

For calibration of the ADVIA Centaur CKMB assay, use the ADVIA Centaur CKMB Calibrator. Perform that calibration as described in the calibrator instructions for use.

Calibration Frequency

Calibrate the assay at the end of the 28-day calibration interval.

Additionally, the ADVIA Centaur 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.

Performing Master Curve Calibration

The ADVIA Centaur 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.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

For detailed information about entering quality control values, refer to the system operating instructions.

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). A satisfactory level of performance is achieved when the analyte values obtained are within the Acceptable Control Range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme.

Taking Corrective Action

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.

Results

Calculation of Results

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

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

Dilutions

The following information pertains to 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 or prepared manually.
- For automatic dilutions, ensure that ADVIA Centaur CKMB Diluent is loaded and set the system parameters as follows:

Dilution point: $\leq 300 \text{ ng/mL}$ (3.75 nmol/L)

Dilution factor: 2, 10

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

- Manually dilute the patient samples when patient results exceed the linearity of the assay using automatic dilution, or when laboratory protocol requires manual dilution.
- Use CKMB Diluent to manually dilute patient samples, and then load the diluted sample in the sample rack, replacing the undiluted sample.
- Ensure that results are mathematically corrected for dilution. If a dilution factor is entered when scheduling the test, the system automatically calculates the result.

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:

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

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.

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.

Expected Values

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 confirmed for the ADVIA Centaur CKMB assay by analyzing 230 serum samples in the range of 0.21 to 268.82 ng/mL (0.00 to 3.36 nmol/L). Refer to *Method Comparison*.

As with all diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.¹⁴

Performance Characteristics

Analytical Measuring Range

The ADVIA Centaur CKMB assay measures CK-MB concentrations from 0.18–300 ng/mL (0.0023–3.75 nmol/L).

Specificity

The cross-reactivity of the ADVIA Centaur CKMB 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.

Cross-reactant	CK-MB value without cross-reactant		CK-MB value with 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
	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 determined according to CLSI Document EP7-A2.¹⁵

Sensitivity

The ADVIA Centaur 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.

Precision

Four samples were assayed 6 times, in each of 24 runs, on 6 systems, (n = 144 for each sample), over a period of 2 days. The following results were obtained:

Mean (ng/mL)	Mean (nmol/L)	Within-run% CV	Run-to-run% CV	Total % CV
3.55	0.0444	2.55	2.96	3.91
28.30	0.3538	2.27	2.89	3.67
80.16	1.0020	2.36	2.81	3.67
114.65	1.4331	2.60	3.55	4.41

Accuracy / Method Comparison

For 230 samples in the range of 0.21 to 268.82 ng/mL (0.00 to 3.36 nmol/L), the relationship between the ADVIA Centaur CKMB assay and the ACS:180 CKMB II assay is described by the equation:

$$\text{ADVIA Centaur CKMB} = 1.03 (\text{ACS:180 CKMB II}) - 0.1 \text{ ng/mL}$$

Correlation coefficient (r) = 0.99

Interferences

Serum specimens that are . . .	Have an insignificant effect on the assay up to . . .
hemolyzed	150 mg/dL of hemoglobin
lipemic	1000 mg/dL of triglycerides
icteric	40 mg/dL of bilirubin

Dilution Recovery

Four human serum samples in the range of 210.03 to 246.54 ng/mL (2.63 to 3.08 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 74.8% to 87.1% with a mean of 80.6%.

Sample	Dilution	Observed (ng/mL)	Expected (ng/mL)	Observed (nmol/L)	Expected (nmol/L)	Recovery %
1	—	246.54		3.08		
	1:2	106.77	123.27	1.33	1.54	86.6
	1:4	51.80	61.63	0.65	0.77	84.1
	1:8	24.39	30.82	0.30	0.39	79.1
	1:16	12.47	15.41	0.16	0.19	81.0
	Mean					82.7
2	—	210.03		2.63		
	1:2	90.06	105.02	1.13	1.31	85.8
	1:4	41.82	52.51	0.52	0.66	79.7
	1:8	20.37	26.25	0.25	0.33	77.6
	1:16	9.81	13.13	0.12	0.16	74.8
	Mean					79.5
3	—	216.59		2.71		
	1:2	94.29	108.30	1.18	1.35	87.1
	1:4	43.44	54.15	0.54	0.68	80.2
	1:8	21.50	27.07	0.27	0.34	79.4
	1:16	10.86	13.54	0.14	0.17	80.2
	Mean					81.7

Sample	Dilution	Observed (ng/mL)	Expected (ng/mL)	Observed (nmol/L)	Expected (nmol/L)	Recovery %
4	—	227.94		2.85		
	1:2	95.78	113.97	1.20	1.42	84.0
	1:4	44.40	56.98	0.56	0.71	77.9
	1:8	21.60	28.49	0.27	0.36	75.8
	1:16	10.81	14.25	0.14	0.18	75.9
	Mean					78.4
Mean						80.6

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

Sample	Amount Added (ng/mL)	Observed (ng/mL)	Amount Added (nmol/L)	Observed (nmol/L)	Recovery %
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
	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

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).

Standardization

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

Technical Assistance

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














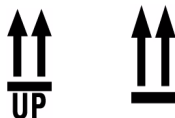










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References

1. Chapman JF, Silverman LM. Cardiac disease and hypertension. In: Kaplan LA, Pesce AJ, editors. *Clinical chemistry: theory, analysis, and correlation*. 2nd ed. St. Louis: CV Mosby, 1989. 415–26.
2. Moss DW, Henderson AR, Kachmar JF. Enzymes. In: Tietz NW, editor. *Fundamentals of clinical chemistry*. 3rd ed. Philadelphia: WB Saunders, 1987. 346–421.
3. BLOMACS Study Group. Early diagnosis and exclusion of acute myocardial infarction using biochemical monitoring. *Coron Artery Dis*. 1995 Apr;6:4.
4. Mair J, Arther DE, Dienstl A, et al. Early detection of acute myocardial infarction by measurement of mass concentration of creatine kinase-MB. *Am J Cardiol*. 1991;68: 1545–50.
5. Apple FS. Acute myocardial infarction and coronary reperfusion. Serum cardiac markers for the 1990s. *Am J Clin Pathol*. 1992;97(2):217–26.
6. Abdelmeguid AE, Whitlow PL, Sapp SK, et al. Long-term outcome of transient, uncomplicated in-laboratory coronary artery closure. *Circulation*. 1995;91(11):2733–41.
7. Chapman JF, Silverman LM. Creatine kinase in the diagnosis of myocardial disease. *Bull Lab Med (NCMH)*. 1982;60:1–7.
8. Silverman LM, Chapman JF, Daasch VN. Isoenzymes. In: Kaplan LA, Pesce AJ, editors. *Clinical chemistry: theory, analysis, and correlation*. 2nd ed. St. Louis: CV Mosby, 1989. 787–94.
9. Wa AH, Wang XM, Gornet TG, et al. Creatine kinase MB isoforms in patients with skeletal muscle injury: ramifications for early detection of acute myocardial infarction. *Clin Chem*. 1992;38:396–400.
10. Larca LJ, Coppola JT, Honig S. Creatine kinase MB isoenzyme in dermatomyositis: A non cardiac source. *Ann Int Med*. 1981;94:341–3.
11. Yasmineh WG, Ibrahim GA, Abbasnezhad M, et al. Isoenzyme distribution of creatine kinase and lactate dehydrogenase in serum and skeletal muscle in Duchenne muscular dystrophy, collagen disease, and other muscular disorders. *Clin Chem*. 1978;24:1985–9.
12. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Handling and Processing of Blood Specimens; Approved Guideline-Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2004. NCCLS Document H18-A3.
13. Boscatto LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem*. 1988;34:27–33.
14. Clinical and Laboratory Standards Institute (formerly NCCLS). *How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline-Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2000. NCCLS Document C28-A2.
15. Clinical and Laboratory Standards Institute (formerly NCCLS). *Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. NCCLS Document EP7-A2.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
	<i>In vitro</i> diagnostic medical device	 REF	Catalog number
	Legal manufacturer		Authorized Representative in the European Community
	CE Mark		CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat		Up
	Use by		Contains sufficient for (n) tests
	Batch code		Shake the reagent pack vigorously. Refer to <i>Preparing Reagents</i> in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	Rev.	Revision
	Master Curve Definition		Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
	Lot Details		Green dot
	Recycle		Printed with soy ink

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