Key to Symbols

CONTAINS: AZIDE	Contains sodium azide. Contact with acids liberates very toxic gas.
DANGER: REPRODUCTIVE HAZARD	Danger: Reproductive Hazard
FOR USE WITH	Identifies products to be used together
IVD	*In Vitro* Diagnostic Medical Device
LOT	Batch code/Lot number
PRODUCT OF ITALY	Product of Italy
R1	Reagent 1
R2	Reagent 2
REF	Catalog number/List number
SN	Serial number
	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date

CK-MB
REF 6K25-30

Customer Service: Contact your local representative or find country-specific contact information on www.abbottdiagnostics.com.

SENTINEL CH. SpA
Via Robert Koch, 2
Milan 20152 Italy

March 2017

Abbott

CK-MB

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Read Highlighted Changes: Revised March 2017.

INTENDED USE

The MULTIGENT CK-MB assay is intended for the kinetic determination of the CK-MB and CK-BB isoenzymes of creatine kinase in serum or plasma on the ARCHITECT *c* Systems.

SUMMARY AND EXPLANATION OF TEST

Creatine kinase (CK) catalyzes the reversible phosphorylation of creatine by ATP. CK is a dimer composed of two subunits which form three active isoenzymes: BB (CK-1), MB (CK-2), and MM (CK-3). CK-BB isoenzyme only rarely appears in serum. Elevated CK values are due to muscle damage and associated pathologies. CK determination, usually performed with CK2 (also called CK-MB), is used for the diagnosis and follow-up of AMI (acute myocardial infarction) and some muscle diseases.

PRINCIPLES OF PROCEDURE

Creatine kinase catalyzes the reaction between creatine phosphate and ADP with formation of creatine and ATP. The ATP formed, in the presence of glucose and hexokinase (HK), yields ADP and glucose-6-phosphate. The glucose-6-phosphate formed in the presence of glucose-6-phosphate dehydrogenase (G6P-DH) reacts with β-$NADP^+$ forming 6-phosphogluconate and β-NADPH. The presence of mouse antibodies that inhibit CK-MM activity in the reaction mixture allows the determination of the residual activity of CK-B isoenzymes (CK-MB and CK-BB). The CK-MB activity is obtained by multiplying the CK-B activity by two. By measuring the variation of the absorbance due to transformation of β-$NADP^+$ into β-NADPH in a time interval at 340 nm, it is possible to calculate the residual activity in the examined sample.
Methodology: IFCC Method/Immunoinhibition

REAGENTS

Reagent Kit

REF 6K25-30 MULTIGENT CK-MB is supplied as a liquid, ready-to-use, two-reagent kit which contains:

R1 2 x 53 mL
R2 2 x 16 mL

Estimated tests per kit: 500

Calculation is based on the minimum reagent fill volume per kit.

Reactive Ingredients		Concentration
R1	Imidazole buffer (pH 6.1)	125 mmol/L
	Glucose	25 mmol/L
	N-acetyl-*L*-cysteine	25 mmol/L
	Hexokinase (phosphorylating)	≥ 52 µkat/L
	EDTA	2.5 mmol/L
	Magnesium acetate	12.5 mmol/L
	NADP	2.5 mmol/L
	Anti-CK-M monoclonal antibodies (mouse)	≥ 2,000 U/L
R2	Creatine phosphate (pH 9.5)	100 mmol/L
	ADP	10 mmol/L
	AMP	25 mmol/L
	Diadenosine 5-phosphate	0.05 mmol/L
	G6P-DH	≥ 125 µkat/L

Nonreactive Ingredients: R1 and R2 contain sodium azide (< 0.1%).

REAGENT HANDLING AND STORAGE

Reagent Handling

- R1 Ready for use.
- R2 Ready for use.
- Remove air bubbles, if present in the reagent cartridge, with a new applicator stick. Alternatively, allow the reagent to sit at the appropriate storage temperature to allow the bubbles to dissipate. To minimize volume depletion, do not use a transfer pipette to remove the bubbles.

  CAUTION: Reagent bubbles may interfere with proper detection of reagent level in the cartridge, causing insufficient reagent aspiration that could impact results.

en
CK-MB
REF 6K25-30
307233/R04
B6K250
FOR USE WITH
ARCHITECT

Reagent Storage

- Unopened reagents are stable until the expiration date when stored at 2 to 8°C.
- Reagent stability is 42 days if the reagent is uncapped and onboard.

Indications of Deterioration

The reagents must be clear; do not use if turbid. Instability or deterioration should be suspected if there are visible signs of leakage, extreme turbidity, microbial growth, if calibration does not meet the appropriate package insert and/or **ARCHITECT System Operations Manual** criteria, or if controls do not meet the appropriate criteria.

WARNINGS AND PRECAUTIONS

Precautions for Users

- IVD
- For *In Vitro* Diagnostic Use.
- Do not use components beyond the expiration date.
- Do not mix materials from different kit lot numbers.
- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens.[1] Biosafety Level 2[2] or other appropriate biosafety practices[3,4] should be used for materials that contain or are suspected of containing infectious agents.
- The following warnings and precautions apply to R1:

  DANGER: Contains imidazole and sodium azide.
  H360 May damage fertility or the unborn child.
  EUH032 Contact with acids liberates very toxic gas.
  Prevention
  P201 Obtain special instructions before use.
  P280 Wear protective gloves / protective clothing / eye protection.
  Response
  P308+P313 If exposed or concerned: Get medical advice / attention.
  Disposal
  P501 Dispose of contents / container in accordance with local regulations.
- The following warnings and precautions apply to R2:
  Contains sodium azide.
  EUH032 Contact with acids liberates very toxic gas.
  P501 Dispose of contents / container in accordance with local regulations.
- Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.
- For a detailed discussion of safety precautions during system operation, refer to the **ARCHITECT System Operations Manual,** *Section 8.*

SPECIMEN COLLECTION AND HANDLING

Suitable Specimens

- **Serum:** Use serum collected by standard venipuncture techniques into plastic tubes with or without gel barriers. Ensure complete clot formation has taken place prior to centrifugation. Centrifuge according to tube manufacturer's instructions to ensure proper separation of serum from blood cells. Glass tubes were not tested.

  Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may take longer to complete their clotting processes. Fibrin clots may subsequently form in these sera and the clots could cause erroneous test results.
- **Plasma:** Use plasma collected by standard venipuncture techniques into plastic tubes. The acceptable anticoagulants are lithium heparin with gel barrier and EDTA. Ensure centrifugation is adequate to remove platelets. Centrifuge according to tube manufacturer's instructions to ensure proper separation of plasma from blood cells. Glass tubes were not tested.

NOTE: Do not use hemolyzed samples.

For total sample volume requirements, refer to the ASSAY PARAMETERS section of this package insert and *Section 5* of the **ARCHITECT System Operations Manual**.

Specimen Storage

Serum and Plasma

Temperature	Maximum Storage	Bibliographic Reference
20 to 25°C	2 days	5
2 to 8°C	7 days	5, 6
-20°C	4 weeks	5

Guder et al.[5] suggest storage of frozen specimens at -20°C for no longer than the time interval cited above. However, limitations of laboratory equipment make it necessary in practice for clinical laboratories to establish a range around -20°C for specimen storage. This temperature range may be established from either the freezer manufacturer's specifications or your laboratory standard operating procedure(s) for specimen storage.

NOTE: Stored specimens must be inspected for particulates. If present, mix and centrifuge the specimen to remove particulates prior to testing.

PROCEDURE

Materials Provided

REF 6K25-30 MULTIGENT CK-MB Kit

Materials Required but not Provided

- REF 6K25-10 MULTIGENT CK-MB Calibrator
- REF 6K25-20 MULTIGENT CK-MB Control
- Saline (0.85% to 0.90% NaCl) for specimens that require dilution

Assay Procedure

For a detailed description of how to run an assay on the ARCHITECT *c* Systems, refer to *Section 5* of the **ARCHITECT System Operations Manual**.

Specimen Dilution Procedure

The ARCHITECT *c* Systems have an automatic dilution feature; refer to *Section 2* of the **ARCHITECT System Operations Manual** for additional information.

Serum and Plasma: Specimens with CK-MB values exceeding 1,000 U/L (16.67 µkat/L) are flagged and may be diluted by following either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

If using the Automated Dilution Protocol, the system performs a dilution of the specimen and automatically corrects the concentration by multiplying the result by the appropriate dilution factor.

Manual Dilution Procedure

- Use saline (0.85% to 0.90% NaCl) to dilute the sample.
- The operator must enter the dilution factor in the patient or control order screen. The system uses this dilution factor to automatically correct the concentration by multiplying the result by the entered factor.
- If the operator does not enter the dilution factor, the result must be multiplied by the appropriate dilution factor before reporting the result.

NOTE: If a diluted sample result is flagged indicating it is less than the linear low limit, do not report the result. Rerun using an appropriate dilution.

For detailed information on ordering dilutions, refer to *Section 5* of the **ARCHITECT System Operations Manual**.

CALIBRATION

Calibration is stable for 42 days (1,008 hours) and is required with each change in reagent lot number. Verify calibration curve with at least two levels of controls according to the established quality control requirements for your laboratory. If control results fall outside acceptable ranges, recalibration may be necessary.

For a detailed description of how to calibrate an assay, refer to *Section 6* of the **ARCHITECT System Operations Manual**.

For information on calibrator standardization, refer to the REF 6K25-10 MULTIGENT CK-MB Calibrator package insert.

QUALITY CONTROL

As appropriate, refer to your laboratory standard operating procedure(s) and/or quality assurance plan for additional quality control requirements and potential corrective actions:

- Two levels of controls (normal and abnormal) are to be run every 24 hours.
- If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.
- If quality control results do not meet the acceptance criteria defined by your laboratory, patient values may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary.
- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

RESULTS

Refer to *Appendix C* of the **ARCHITECT System Operations Manual** for information on results calculations.

To convert results from U/L to µkat/L, multiply U/L by 0.01667.[7]

Representative performance data are given in the EXPECTED VALUES and SPECIFIC PERFORMANCE CHARACTERISTICS sections of this package insert. Results obtained in individual laboratories may vary.

LIMITATIONS OF THE PROCEDURE

CK-MM activities up to 2,000 U/L (33.34 µkat/L) are completely inhibited. Therefore, samples with total CK activities above 2,000 U/L (33.34 µkat/L) require dilution because complete inhibition is no longer assured.

Sulfasalazine at elevated (200 mg/L) levels may lead to falsely low results.

Refer to the SPECIMEN COLLECTION AND HANDLING and SPECIFIC PERFORMANCE CHARACTERISTICS sections of this package insert.

EXPECTED VALUES

Reference Range

	Range (U/L)	Range (µkat/L)
Serum[8] and Plasma	< 25	< 0.42

It is recommended that each laboratory establish its own reference range based upon its particular locale and population characteristics.

For diagnostic purposes, the patient's medical history and other clinical findings should be considered when evaluating CK-MB results.

SPECIFIC PERFORMANCE CHARACTERISTICS

Reportable Range

The reportable range (analytical measurement range) for MULTIGENT CK-MB is 3 to 1,000 U/L (0.05 to 16.67 µkat/L).

Limit of Detection (LOD)

The LOD for MULTIGENT CK-MB is 3 U/L (0.05 µkat/L). The LOD sensitivity for MULTIGENT CK-MB was calculated on 20 replicates of normal saline and reported as the mean zero value + 3 SD.

Interfering Substances

Interference studies were conducted using an acceptance criteria of ± 10% or 2.5 U/L deviation, whichever is greater, from the target value. MULTIGENT CK-MB assay is not affected by the presence of the following interferents up to the concentrations indicated below.

Interfering Substance	Interferent Concentration
Ascorbic acid	60 mg/dL (3,406.8 µmol/L)
Bilirubin, conjugated	6.6 mg/dL (113 µmol/L)
Bilirubin, unconjugated	53 mg/dL (906 µmol/L)
Intralipid	600 mg/dL (6 g/L)
Sulfapyridine	300 mg/L (1204.8 µmol/L)
Temozolomide	20 mg/L (103.1 µmol/L)

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Precision

The precision of the MULTIGENT CK-MB assay is ≤ 7.5% Total CV for concentrations > 25 U/L (0.42 µkat/L) and SD ≤ 2.5 U/L (0.04 µkat/L) for concentrations < 25 U/L (0.42 µkat/L). Studies were performed using Clinical and Laboratory Standards Institute (CLSI) protocol NCCLS EP5-A.[9] Representative results are summarized below.

Control		Level 1	Level 2	Level 3
N		80	80	80
Mean (U/L)		7.3	30.1	79.3
Within Run	SD	0.58	0.49	0.54
	%CV	7.9	1.6	0.9
Between Run	SD	0.14	0.14	0.46
	%CV	1.9	0.5	0.4
Total	SD	0.64	0.57	0.33
	%CV	8.7	1.9	1.7

Method Comparison

Correlation studies were performed using CLSI protocol NCCLS EP9-A.[10] Serum results from the MULTIGENT CK-MB assay on an ARCHITECT *c* System were compared with the results from a commercially available methodology.

Serum results from the MULTIGENT CK-MB assay on an ARCHITECT *c* System were compared with the results on the AEROSET System.

	ARCHITECT vs. Comparative Method	ARCHITECT vs. AEROSET
N	75	60
Y - Intercept	0.14	-0.87
Correlation Coefficient	0.992	0.999
Slope	1.04	0.98
Range (U/L)	4.5 to 231.3	3.9 to 648.0

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TRADEMARKS

ARCHITECT *c* Systems Assay Parameters

CK-MB Serum/Plasma—Conventional and SI Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: **CKMB** Type: **Photometric** Version: †
Number: **2979**
Run controls for onboard reagents by:* **Lot**

● Reaction definition O Reagent / Sample O Validity checks

Reaction mode: **Rate up**

	Primary	Secondary		Read times
Wavelength:	**340**	/ ******	Main:	**28 – 33**
Last required read:	**33**		Flex:	___ – ___
Absorbance range:	**-0.1000 – 1.7000**		Color correction:	___ – ___
Sample blank type:	**None**			

O Reaction definition ● Reagent / Sample O Validity checks

			R1	R2
Reagent:	**CKMB9**	Reagent volume:	**180**	**45**
Diluent:	**Saline**	Water volume:	___	___
Diluent dispense mode:	**Type 0**	Dispense mode:	**Type 0**	**Type 0**

Dilution name	Sample	Diluted sample	Diluent	Water		Dilution factor	Default dilution
STANDARD :	**11.0**	___	___	___	=	**1:1.00**	●
DIL 1 :	**10.0**	**11.0**	**90**	___	=	**1:10.00**	O

O Reaction definition O Reagent / Sample ● Validity checks

Reaction check: **None**

Rate linearity %: **10**

Configure assay parameters — Calibration

O General ● Calibration O SmartWash O Results O Interpretation

Assay: **CKMB** Calibration method: **Linear**

● Calibrators O Volumes O Intervals O Validity checks

Calibrator set:		Calibrator level:	Concentration:
CKMC	Blank:	**Water**	**0.00**‡
	Cal 1:	**CKMC1**	‡‡

Replicates: **3** [Range 1 – 3]

O Calibrators ● Volumes O Intervals O Validity checks

Calibrator: **CKMC**

	Calibrator level	Sample	Diluted sample	Diluent	Water
Blank:	**Water**	**11.0**	___	___	___
Cal 1:	**CKMC1**	**11.0**	___	___	___

O Calibrators O Volumes ● Intervals O Validity checks

Calibration intervals:
Full interval: **1008** (hours)
Calibration type:
Adjust type: **None**

O Calibrators O Volumes O Intervals ● Validity checks

Blank absorbance range: **-0.0100** – **0.0100**
Span: **Blank** – **Blank**
Span absorbance range: _____ – _____
Expected cal factor: **0.00**
Expected cal factor tolerance %: **0**

Configure assay parameters — SmartWash

O General O Calibration ● SmartWash O Results O Interpretation

Assay: **CKMB**

COMPONENT	REAGENT / ASSAY	WASH	Volume	Replicates
R1	**DIG00**	**Detergent A**	**345**	**1**
R1	**AMIK9**	**Detergent A**	**345**	**1**
R1	**VANCO**	**Detergent A**	**345**	**1**
R1	**GENT9**	**Detergent A**	**345**	**1**
R1	**TOBRA**	**Detergent A**	**345**	**1**
R1	**DGT0B**	**Detergent A**	**345**	**1**
R2	**DIG00**	**Detergent A**	**345**	**1**
R2	**AMIK9**	**Detergent A**	**345**	**1**
R2	**VANCO**	**Detergent A**	**345**	**1**
R2	**GENT9**	**Detergent A**	**345**	**1**
R2	**TOBRA**	**Detergent A**	**345**	**1**
R2	**DGT0B**	**Detergent A**	**345**	**1**
Cuvette	**Trig*****	**10% Detergent B**	**345**	

*****Not required for ARCHITECT Software version 7.00 and above.**

CK-MB Serum/Plasma—Conventional Units

Configure assay parameters — Results

O General O Calibration O SmartWash ● Results O Interpretation

Assay: **CKMB** Assay number: **2979**
Dilution default range: Result units: **U/L**
Low-Linearity: **3**
High-Linearity: **1000**
Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME
Either	**0 – 130 (Y)**	**0 – 24**	

Configure result units

Assay: **CKMB**
Version: †
Result units: **U/L**
Decimal places: **0** [Range 0 – 4]
Correlation factor: **1.0000**
Intercept: **0.0000**

CK-MB Serum/Plasma—SI Units

Configure assay parameters — Results

O General O Calibration O SmartWash ● Results O Interpretation

Assay: **CKMB** Assay number: **2979**
Dilution default range: Result units: **ukat/L**
Low-Linearity: **0.05**
High-Linearity: **16.67**
Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME
Either	**0 – 130 (Y)**	**0.00 – 0.40**	

Configure result units

Assay: **CKMB**
Version: †
Result units: **ukat/L**
Decimal places: **2** [Range 0 – 4]
Correlation factor: **1.0000**
Intercept: **0.0000**

† Due to differences in instrument systems and unit configurations, version numbers may vary.
* Parameter is available in ARCHITECT Software version 7.00 and above.
** *c*8000 Secondary Wavelength is 444 nm; *c*4000 and *c*16000 Secondary Wavelength is 450 nm.
‡ Displays the number of decimal places defined in the decimal places parameter field.
‡‡ Refer to the concentration specified on calibrator labeling or value sheet. In ARCHITECT Software version 5.00 and above, these values are defined on the Configure calibrator set screen.

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