BECKMAN COULTER

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SYNCHRON® System(s) Chemistry Information Sheet

CK Creatine Kinase

REF 442635 (200 tests/cartridge)
REF 476836 (400 tests/cartridge)

For *In Vitro* Diagnostic Use

ANNUAL REVIEW

Reviewed by:	Date	Reviewed by:	Date

PRINCIPLE

INTENDED USE

CK reagent, when used in conjunction with SYNCHRON LX® System(s), UniCel® DxC 600/800 System(s), is intended for the quantitative determination of creatine kinase activity in human serum or plasma.

CLINICAL SIGNIFICANCE

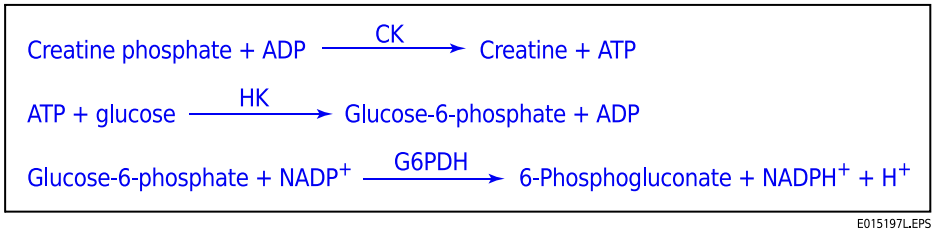
Measurements of creatine kinase and its isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

METHODOLOGY

CK reagent is used to measure the CK activity by an enzymatic rate method.[1,2,3,4] In the reaction creatine kinase catalyzes the transfer of a phosphate group from the creatine phosphate substrate to adenosine diphosphate (ADP). The subsequent formation of adenosine triphosphate (ATP) is measured through the use of two coupled reactions catalyzed by hexokinase (HK) and glucose-6-phosphate dehydrogenase (G6PDH) which results in the production of reduced β-nicotinamide adenine dinucleotide phosphate (NADPH) from β-nicotinamide adenine dinucleotide phosphate (NADP). The CK assay contains the activator monothioglycerol.

The SYNCHRON® System(s) automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 20 parts reagent. The system monitors the change in absorbance at 340 nanometers. This change in absorbance is directly proportional to the activity of CK in the sample and is used by the System to calculate and express CK activity.

CHEMICAL REACTION SCHEME



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SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.[5] Freshly drawn serum or plasma are the preferred specimens. Acceptable anticoagulants are listed in the PROCEDURAL NOTES section of this chemistry information sheet. Whole blood or urine are not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum or plasma be physically separated from contact with cells within two hours from the time of collection.[6]
2. Stability of CK activity in sera is not well defined, but is generally poor. Specimens should be assayed as soon after collection as possible since activity loss may occur after specimens have been stored for 4 hours at room temperature, 8 to 12 hours refrigerated or 2 to 3 days when frozen.[6]

Additional specimen storage and stability conditions as designated by this laboratory:

SAMPLE VOLUME

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes and minimum volumes, refer to the Primary Tube Sample Template for your system.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet for information on unacceptable specimens.

Criteria for sample rejection as designated by this laboratory:

PATIENT PREPARATION

Special instructions for patient preparation as designated by this laboratory:

SPECIMEN HANDLING

Special instructions for specimen handling as designated by this laboratory:

REAGENTS

CONTENTS

Each kit contains the following items:

Two Creatine Kinase Reagent Cartridges (2 x 200 tests) or (2 x 400 tests and two bottles of CK [A-reagent])

VOLUMES PER TEST

Sample Volume	13 µL
ORDAC Sample Volume	3 µL
Total Reagent Volume	260 µL
Cartridge Volumes	
A	238 µL
B	22 µL
C	– –

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS	
Creatine phosphate	53 mmol/L
Glucose	18 mmol/L
ADP	2.9 mmol/L
NAD^+	2.4 mmol/L
Hexokinase	>11 KIU/L
Glucose-6-phosphate dehydrogenase	>3.8 KIU/L

Also non-reactive chemicals necessary for optimal system performance.

Avoid skin contact with reagent. Use water to wash reagent from skin.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

At least two levels of control material
Saline

REAGENT PREPARATION

For P/N 442635 (200 tests): Transfer the entire contents of the smallest reagent compartment (C) into the largest reagent compartment (A).
For P/N 476836 (400 tests): Transfer all the contents of one bottle CK (A-reagent) into the largest reagent compartment (A).
Replace cartridge caps and gently invert the cartridge several times to ensure adequate mixing.

ACCEPTABLE REAGENT PERFORMANCE

The acceptability of a reagent is determined by ensuring that quality control results are within your facility's acceptance criteria.

REAGENT STORAGE AND STABILITY

CK reagent, when stored unopened at +2°C to +8°C, will remain stable until the expiration date printed on the cartridge label. Once prepared, the reagent cartridge is stable for 30 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

Reagent storage location:

CALIBRATION

CALIBRATOR REQUIRED

Calibration is not required.

TRACEABILITY

This measurand (analyte) is traceable to the manufacturer's selected Measurement Procedure as described in the Methodology section.

QUALITY CONTROL

At least two levels of control material, normal and abnormal, should be analyzed daily. In addition, these controls should be run with each new reagent cartridge and after specific maintenance or troubleshooting procedures as detailed in the appropriate system manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.

The following controls should be prepared and used in accordance with the package inserts. Discrepant quality control results should be evaluated by your facility.

Table 1.0 Quality Control Material

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

1. If necessary prepare reagent as defined in the Reagent Preparation section of this chemistry information sheet and load the reagent onto the system.
2. Program samples and controls for analysis.
3. After loading samples and controls onto the system, follow the protocols for system operations.

For detailed testing procedures, refer to the SYNCHRON LX *Operations Manual*, or the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

CALCULATIONS

The SYNCHRON® System(s) performs all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

REPORTING RESULTS

Equivalency between the SYNCHRON LX and UniCel DxC 600/800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The following reference intervals were taken from literature and a study performed on SYNCHRON Systems.[7]

Table 2.0 Reference intervals

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Literature	Serum or Plasma (Male)	38 – 174 IU/L	0.65 – 2.96 µkat/L
	Serum or Plasma (Female)	26 – 140 IU/L	0.46 – 2.38 µkat/L
SYNCHRON	Serum or Plasma (Male)	49 – 397 IU/L	0.83 – 6.75 µkat/L
	Serum or Plasma (Female)	38 – 234 IU/L	0.65 – 3.98 µkat/L

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Laboratory			

Refer to References (8,9,10) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

1. If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method based on a study of 20 healthy volunteers:

Table 3.0 Acceptable Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	AVERAGE PLASMA-SERUM BIAS (IU/L)[a]
Ammonium Heparin	29 Units/mL	NSI[b]
Sodium Heparin	29 Units/mL	NSI
Lithium Heparin	29 Units/mL	NSI

a Bias is based on worst case instead of average.
b NSI = No Significant Interference (within ±10.0 IU/L or 7%).

2. The following anticoagulants were found to be incompatible with this method:

Table 4.0 Incompatible Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	PLASMA-SERUM BIAS (IU/L)[a]
Potassium Oxalate/Sodium Fluoride	4.0 / 5.0 mg/mL	-80.0
Sodium Citrate	6.6 mg/mL	-97.0

a Bias is based on worst case instead of average. Plus (+) or minus (-) signs in this column signify positive or negative bias.

LIMITATIONS

None identified.

INTERFERENCES

1. The following substances were tested for interference with this methodology:

Table 5.0 Interferences[a]

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT[b]
Bilirubin (unconjugated)	Bovine	30 mg/dL	NSI[c]
Hemoglobin	RBC hemolysate	50 mg/dL	+12 IU/L
Lipemia	Intralipid[d]	500 mg/dL	NSI
Adenylate Kinase	NA[e]	100 U/L	+8 IU/L

a Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.
b Plus (+) or minus (-) signs in this column signify positive or negative interference.
c NSI = No Significant Interference (within ± 10 IU/L or 7%).
d Intralipid is a registered trademark of KabiVitrum, Inc., Clayton, NC 27250.
e NA = Not applicable.

2. Refer to References (11,12,13) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

ANALYTIC RANGE

The SYNCHRON® System(s) method for the determination of this analyte provides the following analytical ranges:

Table 6.0 Analytical Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum or Plasma	5–1200 IU/L	0.1–20.0 µkat/L
Serum or Plasma (ORDAC)[a]	860–4100 IU/L	14.3–68.3 µkat/L

a Overrange Detection and Correction. Refer to the SYNCHRON LX *Operations Manual*, or the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual for more details on this function.

Samples with activities exceeding the high end of the analytical range should be rerun with ORDAC enabled or diluted with saline and reanalyzed.

REPORTABLE RANGE (AS DETERMINED ON SITE):

Table 7.0 Reportable Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS

SENSITIVITY

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for CK determination is 5 IU/L (0.08 µkat/L).

EQUIVALENCY

Equivalency was assessed by Deming regression analysis of patient samples to accepted clinical methods.

Serum or plasma (in the range of 10 to 1126 IU/L):

Y (SYNCHRON LX Systems)	= 1.025X + 0.39
N	= 80
MEAN (SYNCHRON LX Systems)	= 286.5
MEAN (SYNCHRON CX7 DELTA)	= 279.1
CORRELATION COEFFICIENT (r)	= 0.9991

Refer to References (14) for guidelines on performing equivalency testing.

PRECISION

A properly operating SYNCHRON® System(s) should exhibit precision values less than or equal to the following:

Table 8.0 Precision Values

TYPE OF PRECISION	SAMPLE TYPE	1 SD		CHANGEOVER VALUE[a]		% CV
		IU/L	µkat/L	IU/L	µkat/L	
Within-run	Serum/Plasma	5.0	0.08	142.9	2.29	3.5
	Serum/Plasma (ORDAC)	NA[b]	NA	NA	NA	10.0
Total	Serum/Plasma	7.5	0.12	142.9	2.29	5.3
	Serum/Plasma (ORDAC)	NA	NA	NA	NA	15.0

a When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test % CV to the guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

b NA = Not applicable.

Refer to References (15) for guidelines on performing precision testing.

Comparative performance data for a SYNCHRON LX® System evaluated using the NCCLS Proposed Guideline EP5-T2 appears in the table below.[15] Each laboratory should characterize their own instrument performance for comparison purposes.

Table 9.0 NCCLS EP5-T2 Precision Estimate Method

TYPE OF IMPRECISION	SAMPLE TYPE		No. Systems	No. Data Points[a]	Test Mean Value (IU/L)	EP5-T2 Calculated Point Estimates	
						SD	%CV
Within-run	Serum	Control 1	1	80	52.3	1.6	3.0
	Serum	Control 2	1	80	630.0	4.8	0.8
	Serum	Human Pool	1	80	258.2	2.9	1.1
Total	Serum	Control 1	1	80	52.3	1.9	3.7
	Serum	Control 2	1	80	630.0	5.7	0.9
	Serum	Human Pool	1	80	258.2	3.4	1.3

a The point estimate is based on the data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer's instructions.

NOTICE

These degrees of precision and equivalency were obtained in typical testing procedures on a SYNCHRON LX® System and are not intended to represent the performance specifications for this reagent.

ADDITIONAL INFORMATION

For more detailed information on SYNCHRON LX Systems or UniCel DxC Systems, refer to the appropriate system manual.

SHIPPING DAMAGE

If damaged product is received, notify your Beckman Coulter Clinical Support Center.

REFERENCES

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