TRAINING UPDATE

Lab Location:	SGMC & WAH	**Date Distributed:**	8/3/2018
Department:	Core Lab	**Due Date:**	8/31/2018
		Implementation:	**8/27/2018**

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:

Creatine Kinase by Dimension Vista® System SGAH.C105 v4

This has been converted to a system SOP

Description of change(s):

Revise QC info and freezer range (to match practice), Most other changes are format updates

Section	Reason
Header	Add WAH
3.2	Remove specimen onboard stability
4,5,6	Remove individual section labeling instructions and add general one
6.1, 6.2	Update QC material and storage
7.2	Add freezer requirements by product
10.5	Move patient review from section 6
10.6	Remove repeat value below AMR/CRR
15	Update to new standard wording
16	Update policy title
17	Update QC product and PI dates

This revised SOP will be implemented on August 27, 2018

Document your compliance with this training update by taking the quiz in the MTS system.

Technical SOP

Title	**Creatine Kinase by Dimension Vista® System**
Prepared by	Ashkan Chini Date: 6/25/2012
Owner	Robert SanLuis Date: 6/11/2014

Laboratory Approval	**Local Effective Date:**	
Print Name and Title	**Signature**	**Date**
Refer to the electronic signature page for approval and approval dates.		

Review		
Print Name	**Signature**	**Date**

Form revised 2/02/2007

TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Local Code
Creatine Kinase	Dimension Vista® System	CPK

Synonyms/Abbreviations
CK, CPK, CKI

Department
Chemistry

Form revised 2/02/2007

2. ANALYTICAL PRINCIPLE

In a coupled enzyme reaction, the creatine kinase in patient samples catalyzes the transphosphorylation of phosphate from creatine phosphate to adenosine diphosphate (ADP) producing adenosine triphosphate (ATP). Hexokinase (HK) phosphorylates glucose from the ATP. The resulting glucose-6-phosphate is oxidized by glucose-6-phosphate dehydrogenase (G-6-PDH) with the simultaneous reduction of nicotinamide adenine dinucleotide phosphate (NADP).

The rate of formation of NADPH is directly proportional to the CK activity in the sample and is measured bichromatically at 340 and 540 nm.

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow[\text{Mg}^{++}\text{, EDTA}]{\text{CK}} \text{Creatine} + \text{ATP}$$

$$\text{ATP} + \text{Glucose} \xrightarrow{\text{HK}} \text{ADP} + \text{Glucose-6-phosphate}$$

$$\text{Glucose-6-phosphate} + \text{NADP}^{+} \xrightarrow[\text{G-6-PDH}]{\text{Mg}^{++}} \text{6-Phosphogluconolactone} + \text{NADPH} + (\text{H}^{+})$$

3. SPECIMEN REQUIREMENTS

3.1 Patient Preparation

Component	Special Notations
Fasting/Special Diets	N/A
Specimen Collection and/or Timing	Normal procedures for collecting and storing serum and plasma may be used for samples to be analyzed by this method.
Special Collection Procedures	N/A
Other	N/A

3.2 Specimen Type & Handling

Criteria	
Type -Preferred **-Other Acceptable**	Plasma (Lithium Heparin) Serum
Collection Container	Plasma: Mint green top tube (PST) Serum: Red top tube, Serum separator tube (SST)
Volume - Optimum **- Minimum**	1.0 mL 0.5 mL
Transport Container and Temperature	Collection container or Plastic vial at room temperature

Criteria		
Stability & Storage Requirements	Room Temperature:	2 hours
	Refrigerated:	7 days
	Frozen:	29 days
Timing Considerations	Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of two hours from the time of collection.	
Unacceptable Specimens & Actions to Take	Specimens that are unlabeled, improperly labeled, or those that do not meet the stated criteria are unacceptable. Request a recollection and credit the test with the appropriate LIS English text code for "test not performed" message. Examples: Quantity not sufficient-QNS; Wrong collection-UNAC. Document the request for recollection in the LIS.	
Compromising Physical Characteristics	Gross hemolysis. Reject sample and request a recollection. Credit the test with the appropriate LIS English text code explanation of HMT (Specimen markedly hemolyzed)	
Other Considerations	Allow Red Top or SST to clot completely prior to centrifugation.	

NOTE: Labeling requirements for all reagents, calibrators and controls include: (1) Open date, (2) Substance name, (3) Lot number, (4) Date of preparation, (5) Expiration date, (6) Initials of tech, and (7) Any special storage instructions. Check all for visible signs of degradation. When placed onboard the analyzer, the instrument captures the date / time loaded and calculates and tracks the opened expiration.

4. REAGENTS

The package insert for a new lot of kits must be reviewed for any changes before the kit is used. A current Package Insert is included as a Related Document.

4.1 Reagent Summary

Reagents	Supplier & Catalog Number
Creatine Kinase	Siemens, Flex® reagent cartridge, Cat. No. K2038

4.2 Reagent Preparation and Storage

Reagent	Creatine Kinase
Container	Reagent cartridge
Storage	Store at 2-8°C
Stability	• Stable until expiration date stamped on reagent cartridges. • Sealed wells on the instrument are stable for 30 days. • Open well stability: o 5 days for wells 1 - 8 o 10 days for wells 9 - 12

Preparation	All reagents are liquid and ready to use.

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
ENZ 6 CAL	Siemens Dimension Vista®, Cat. No. KC360

5.2 Calibrator Preparation and Storage

Calibrator	ENZ 6 CAL
Preparation	Thaw at room temperature to 30 – 45 minutes. Do not thaw in a water bath or water about 25°C. Before use, gently invert the calibrator vials at least ten times to ensure that the contents are thoroughly mixed. **Do not vortex.**
Storage/Stability	• Store at -15°C to -25°C • **Unopened Calibrator:** until expiration date on the box. • **Opened Calibrator:** once the stopper is punctured, stable for 7 days when stored on board the Dimension Vista System.

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	ENZ 6 CAL
Assay Range	7 – 1000 U/L
Suggested Calibration Level	See Reagent Package Insert for lot specific assigned values in U/L
Frequency	• Every new reagent cartridge lot. • Every 90 days for any one lot • When major maintenance is performed on the analyzer. • When control data indicates a significant shift in assay.
Calibration Scheme	2 levels, n = 5

5.4 Calibration Procedure

Auto Calibration:

1. Place the required calibrator vials in a carrier. Make sure the barcode labels are entirely visible through the slots.
2. Place the carrier in the loading area.
3. Position the carrier with the labels facing away from the user.

4. Press the **Load** button.
5. Automatic calibration requires that calibrators be on the instrument. As the time for processing approaches, the instrument reviews onboard inventory for the appropriate calibrators.

Manual Calibration:

1. Verify that calibrators and reagents are in inventory on the instrument.
2. Press **System > Method Summary > Calibration**.
3. Select a method from the sidebar menu. Press the **Order Calibration** button on the screen.
4. Verify that the information on the screen is correct. Verify that the calibrator lot is correct using the drop-down menu.
   a. When calibrating using Vials press **OK**.
   b. When calibrating using Cups, check the Use Cups box. This displays the rack and cup position fields. For additional cups use the positions in ascending order. Be sure to use the number of calibration levels and cups as specified in the method IFU. Scan the rack barcode and place calibrator cups in an adapter in position 1 on a rack. Press **OK** and load the rack on the instrument.
5. The status field in the calibration screen changes sequentially to Awaiting Scheduling, Preparing Calibrators and Processing.

5.5 Tolerance Limits

IF……	THEN……
If result fall within assay-specific specification, and QC values are within acceptable limits,	proceed with analysis
If result falls outside assay-specific specification, or QC values are out of Acceptable limits,	troubleshoot the assay and/or instrument and repeat calibration

6. QUALITY CONTROL

6.1 Controls Used

Controls	Supplier and Catalog Number
Liquid Assayed Multiqual® Levels 1 and 3	Bio-Rad Laboratories Cat. No. 337 and 339

6.2 Control Preparation and Storage

Control	Liquid Assayed Multiqual, Levels 1 and 3
Preparation	Allow the frozen control to stand at room temperature (18-25°C) for 30 minutes or until completely thawed. Swirl the contents gently to ensure homogeneity. (Do not use a mechanical mixer) Use immediately. After each use, promptly replace the stopper and return to 2-8°C storage.

Storage/Stability	**Frozen**: stable until the expiration date at -20 to -50°C. **Thawed and Unopened:** When stored at 2-8°C and the stopper is not punctured, it will be stable for 30 days for CK This product can be used for 7 days when stored on-board the Siemens Dimension Vista at 2-8°C. **Thawed and Opened**: Once the stopper is punctured, all analytes will be stable for 5 days when stored at 2-8°C. Store away from light.

6.3 Frequency

Analyze all levels of QC material after every calibration and each day of testing (notated on the QC frequency sheets posted on the instruments).

Refer to the Dimension Vista® QC Schedule in the Laboratory policy Quality Control Program and in the Dimension Vista® Quick Reference Guide.

6.4 Tolerance Limits and Criteria for Acceptable QC

Step	Action
1	Acceptable ranges for QC are programmed into the instrument's Quality Control software system and Unity Real Time, and may be posted near the instrument for use during computer downtime.
2	**Run Rejection Criteria** • Anytime the established parameters are exceeded (if one QC result exceeds 2 SD), the run is considered out of control (failed) and patient results must not be reported. • The technologist must follow the procedure in the Laboratory QC Program to resolve the problem.
3	**Corrective Action**: • All rejected runs must be effectively addressed through corrective action. Steps taken in response to QC failures must be documented. Patient samples in failed analytical runs must be reanalyzed according to the Laboratory QC Program. Supervisors may override rejection of partial or complete runs only with detailed documentation and criteria for overrides that are approved by the Medical Director. Consult corrective action guidelines in Laboratory QC Program. Follow corrective action guidelines in the Laboratory QC Program. • Corrective action documentation must follow the Laboratory Quality Control Program.

Step	Action
4	**Review of QC** • QC must be reviewed weekly by the Group Lead or designee and monthly by the Supervisor/Manager or designee. • If the SD and/or CV are greater than established ranges, investigate the cause for the imprecision and document implementation of corrective actions.

6.5 Documentation

- QC tolerance limits are programmed into the instrument and Unity Real Time; it calculates cumulative mean, SD and CV and stores all information for easy retrieval.
- Quality control records are reviewed daily at the bench, weekly by the Group Lead or designee, and monthly by the Supervisor/Manager or designee.
- Refer to complete policies and procedures for QC documentation and for record retention requirements in the Laboratory QC Program.

6.6 Quality Assurance Program

- Each new lot number of reagent or new shipment of the same lot of reagent must be tested with external control materials and previously analyzed samples. Performance of the new lot must be equivalent to the previous lot; utilize published TEA for acceptability criteria.
- Training must be successfully completed and documented prior to performing this test. This procedure must be incorporated into the departmental competency assessment program.
- The laboratory participates in CAP proficiency testing. All proficiency testing materials must be treated in the same manner as patient samples.
- Monthly QC must be presented to the Medical Director or designee for review and signature.
- Monthly QC mean and SD are sent to Bio-Rad Laboratories for peer group comparison.
- Consult the Laboratory QC Program for complete details.

7. EQUIPMENT and SUPPLIES

7.1 Assay Platform

Dimension Vista® System

7.2 Equipment

- Refrigerator capable of sustaining 2–8°C.

- Freezer capable of sustaining range to not exceed -15 to -25°C for calibrator.
- Freezer capable of sustaining range not to exceed -20 to -50°C for QC product.
- Centrifuge

7.3 Supplies

- Aliquot Plates
- System Fluids
- Assorted calibrated pipettes (MLA or equivalent) and disposable tips

8. PROCEDURE

CKI Flex® reagent cartridge Cat. No. K2038 is required to perform this test.

Creatine Kinase is performed on the Dimension Vista® System after the method is calibrated (see Reference Material in Calibration section) and Quality Controls are acceptable.

NOTE: For all procedures involving specimens, buttoned lab coats, gloves, and face protection are required minimum personal protective equipment. Report all accidents to your supervisor.

8.1	Sample Processing
1.	A sample rack holding tubes or cups is placed on the rack input lane.
2.	The sample shuttle moves the rack to the barcode reader which identifies the rack and samples to the system.
3.	The rack moves into the sample server and to the rack positioner.
4.	At the same time, aliquot plates move from the aliquot loader into position.
5.	The aliquot probe aspirates the sample from the tubes or cups and dispenses it into the wells of the aliquot plates.
6.	After each aspirate-dispense action, the probe is thoroughly rinsed inside and out to prevent sample carryover.
7.	When sample aspiration is completed, the sample server moves the rack back to the sample shuttle, where it is placed on the output lane and can be removed by the operator.

8.2	Specimen Testing
1.	For QC placement and frequency, refer to the Dimension Vista® QC Schedule in the Laboratory QC Program.
2.	Follow the instructions, outlined in the Dimension Vista® Operator's Manual
3.	The instrument reporting system contains error messages to warn the user of specific malfunctions. Results followed by such error messages should be held for follow-up. Refer to the Dimension Vista® system manual "Error messages" section for troubleshooting.

8.2	Specimen Testing
4.	Follow protocol in Section 10.5 "Repeat criteria and resulting" for samples with results above or below the Analytical Measurement Range (AMR). Investigate any failed delta result and repeat, if necessary.
5.	Append the appropriate English text code qualifier messages to any samples requiring a comment regarding sample quality and/or any other pertinent factors.

Test Conditions	
Sample Volume:	5.9 µL
Reagent 1 Volume:	47.1 µL
Reagent 2 Volume:	23.1 µL
Reaction Time:	9.5 minutes
Test Temperature:	37°C
Wavelength:	340 and 540 nm
Type of measurement:	Bichromatic rate

NOTE: In the event that the test system becomes inoperable, notify supervision or designee for further direction. Patient specimens must be stored in a manner that maintains the integrity of the specimen.

9. CALCULATIONS

The instrument automatically calculates the concentration of Creatine Kinase in U/L.

10. REPORTING RESULTS AND REPEAT CRITERIA

10.1 Interpretation of Data

None required

10.2 Rounding

No rounding is necessary. Instrument reports results as a whole number.

10.3 Units of Measure

U/L

10.4 Clinically Reportable Range (CRR)

7 – 100,000 U/L

Notes: Extended CRR

1) For pediatric samples (patient <18 years), dilute the specimen until a result is obtained.
2) Upon physician special request, specimens can be diluted until a result is obtained.

10.5 Review Patient Data

Each result is reviewed for error messages. Refer to the Dimension Vista system manual "Error messages" section for troubleshooting. Resolve any problems noted before issuing patient reports.

10.6 Repeat Criteria and Resulting

All repeats must replicate the original result within the total allowable error (TEa) of the assay. Refer to TEa listing for specific information.

Values that fall below or within the AMR or CRR may be reported without repeat. Values that exceed the upper ranges must be repeated.

IF the result is …	THEN…
< 7 U/L	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: < 7 U/L
≥ 1,000 U/L	**On Board Automated Dilution:** Results ≥ 1,000 U/L will automatically have repeat testing performed into the instrument using dilution factor of 7 and 14. The instrument first repeats the test using dilution factor of 7. If the obtained result is > 7,000 U/L, it will repeat the test using dilution factor of 14. No multiplication is necessary.
> 14,000 U/L	**Manual Dilution:** Using the primary tube, make the smallest dilution possible to bring the raw data within the AMR. Maximum allowable dilution: x 100 **Notes: Extended CRR** 1) For pediatric samples (patient <18 years), dilute the specimen until a result is obtained. 2) Upon physician special request, specimens can be diluted until a result is obtained. **DILUENT**: Reagent Grade Water Enter dilution factor as a whole number. Re-assay. Readout is corrected for dilution.
> 100,000 U/L	If the recommended dilution does not give results within the clinically reportable range, report as: "> 100,000 U/L-REP" Bring to the attention of your supervisor prior to releasing result. *(See notes above for Extended CRR).*

Message	Code
Verified by repeat analysis	Append –REP to the result.

11. EXPECTED VALUES

11.1 Reference Ranges

Age	Female	Male
Adult (>18 years):	21 – 215 U/L	32 – 232 U/L
Pediatric:		
15 – 18 years	28 - 142	34 - 147
11 – 14 years	31 - 172	31 - 152
2 – 10 years	25 - 177	31 - 152
13 months – 23 months	25 - 177	28 - 162
3 – 12 months	27 - 242	25 - 172
0– 90 days	43 - 474	29 - 303

11.2 Critical Values

None established

11.3 Standard Required Messages

None established

12. CLINICAL SIGNIFICANCE

Measurements of creatine kinase are used in the diagnosis and treatment of myocardial infarction and muscle diseases. Creatine kinase (CK) may also be elevated following muscle injury or strenuous exercise.

13. PROCEDURE NOTES

- **FDA Status:** FDA Approved/cleared
- **Validated Test Modifications:** None

The instrument reporting system contains error messages to warn the operator of specific malfunctions. Any report slip containing such error messages should be held for follow-up. Refer to your Dimension Vista Operator's Guide.

The expected maximum observed standard deviations for repeatability using n = 5 replicates at the following creatine kinase concentrations are:

CKI Concentration	Acceptable S.D. Maximum
107 U/L	5.9 U/L
810 U/L	39.4 U/L

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

7 – 1000 U/L

14.2 Precision

Material	Mean U/L	Standard Deviation (%CV)	
		Repeatability	Within-Lab
Multiqual Unassayed Control			
Level 1	112	1.42 (1.3)	2.70 (2.4)
Level 3	878	9.40 (1.1)	10.25 (1.2)

14.3 Interfering Substances

Hemolysis at 300 mg/dL of hemoglobin increases CKI results by 22% at creatine kinase activities of 192 U/L.

HIL Interference:
The CKI method was evaluated for interference according to CLSI/NCCLS EP7-A2. Bias, defined as the difference between the control sample (does not contain interferent) and the test sample (contains interferent), is shown in the table below. Bias exceeding 10% is considered "interference".

Substance tested	Substance Concentration	CKI U/L	Bias %
Hemoglobin (hemolysate)	300 mg/dL 100 mg/dL	192 491	22 <10
Bilirubin (unconjugated)	80 mg/dL	186, 506	<10
Bilirubin (conjugated)	80 mg/dL	186, 516	<10
Lipemia (Intralipid®)	3000 mg/dL	188, 492	<10

14.4 Clinical Sensitivity/Specificity/Predictive Values

Not available

15. SAFETY

Refer to your local and corporate safety manuals and Safety Data Sheet (SDS) for detailed information on safety practices and procedures and a complete description of hazards.

16. RELATED DOCUMENTS

1. Dimension Vista® Clinical Chemistry System Operator's Manual
2. Dimension Vista® Calibration/Verification Procedure
3. Dimension Vista® Cal Accept Guidelines
4. Dimension Vista® Calibration summary
5. Dimension Vista® Sample Processing, Startup and Maintenance procedure
6. Laboratory Quality Control Program
7. QC Schedule for Siemens Dimension Vista®
8. Laboratory Safety Manual
9. Safety Data Sheets (SDS)
10. Dimension Vista® Limits Chart (AG.F200)
11. Quest Diagnostics Records Management Procedure
12. Dimension Vista® System Error Messages Chart
13. Centrifuge Use, Maintenance and Function Checks (Lab policy)
14. Specimen Acceptability Requirements (Lab policy)
15. Repeat Testing Requirement (Lab policy)
16. Current Allowable Total Error Specifications at http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls
17. Current package insert CKI Flex® Reagent Cartridge K2038

17. REFERENCES

1. Goshal, Amit K. and Soldin, Steven J., Evaluation of the Dade Behring Dimension® RxL: Integrated chemistry system-pediatric reference ranges. Clinica Chimica Acta 2003; 331:144
2. Package Insert, CKI Flex® Reagent Cartridge K2038, Siemens Healthcare Diagnostics Inc., 12/16/2016.
3. Package Insert, ENZ 6 CAL, Siemens Healthcare Diagnostics Inc., 05/2015.
4. Package Insert, Liquid Assayed Multiqual® Chemistry Controls, Bio-Rad Laboratories, 05/2017.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
000	6/11/14		Update owner	L Barrett	R SanLuis
000	6/11/14	10.4, 10.5	Change upper limit of CRR, add instruction for extending for pediatric specimens and special requests	R SanLuis	R SanLuis
000	6/11/14	16	Update titles	L Barrett	R SanLuis
000	6/11/14	Footer	Version # leading zero's dropped due to new EDCS in use as of 10/7/13.	L Barrett	R SanLuis
1	2/4/15	5.2	Change in frozen storage temperature	L Barrett	R SanLuis
1	2/4/15	7.2	Change freezer requirements	L Barrett	R SanLuis
2	4/11/16	3.2	Specify anticoagulant	L Barrett	R SanLuis

Version	Date	Section	Reason	Reviser	Approval
2	4/11/16	4.2	Add safety statement	A Chini	R SanLuis
2	4/11/16	5.2	Remove uncapped calibrator stability	A Chini	R SanLuis
2	4/11/16	6.4, 6.6	Replace LIS with Unity Real Time	L Barrett	R SanLuis
2	4/11/16	10.5	Add explanation of onboard dilution factor, change manual dilution to >14,000	A Chini	R SanLuis
2	4/11/16	17	Update package inserts	A Chini	R SanLuis
3	7/25/18	Header	Add WAH	L Barrett	R SanLuis
3	7/25/18	3.2	Remove specimen onboard stability	L Barrett	R SanLuis
3	7/25/18	4,5,6	Remove individual section labeling instructions and add general one	L Barrett	R SanLuis
3	7/25/18	6.1, 6.2	Update QC material and storage	L Barrett	R SanLuis
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3	7/25/18	15	Update to new standard wording	L Barrett	R SanLuis
3	7/25/18	16	Update policy title	L Barrett	R SanLuis
3	7/25/18	17	Update QC insert, update PI dates	L Barrett	R SanLuis

19. ADDENDA

None