TRAINING UPDATE

Lab Location:	GEC	**Date Distributed:**	5/4/2015
Department:	Core	**Due Date:**	6/1/2015
		Implementation:	**6/1/2015**

DESCRIPTION OF PROCEDURE

Name of procedure:

Cardiac Troponin-I by Dimension® Xpand Chemistry Analyzer GEC.C20 v3

Creatine Kinase by Dimension® Xpand Chemistry Analyzer GEC.C21 v4

Description of change(s):

Cardiac Troponin-I

Section	Reason
1,7.1	Add analyzer name
5.2	Change in frozen storage temperature
6.2	Update stability to 10 days
6.4, 6.6	Replace LIS with Unity Real Time
7.2	Change freezer requirements
8.2	Remove Lynx, specify Xpand process

Creatine Kinase

Section	Reason
5.2	Change in frozen storage temperature and thawed stability
6.4, 6.6	Replace LIS with Unity Real Time
7.2	Change freezer requirements

The revised SOPs will be implemented on June 1, 2015

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

Approved draft for training

Technical SOP

Title	**Cardiac Troponin-I by Dimension® Xpand Chemistry Analyzer**
Prepared by	Ashkan Chini Date: 3/24/2011
Owner	Robert SanLuis Date: 4/2/2015

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
Troponin-I	Dimension® Xpand Chemistry Analyzer	TROPI1

Synonyms/Abbreviations
Cardiac Troponin-I / TROP, TROPI, CTNI Troponin is part of battery/package CIEP4

Department
Chemistry

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2. ANALYTICAL PRINCIPLE

The CTNI method is a one step enzyme immunoassay based on the "sandwich" principle. Sample is incubated with chromium dioxide particles coated with a monoclonal antibody specific for the cardiac troponin-I molecule, and a conjugate reagent [alkaline phosphatase (ALP)] labeled monoclonal antibody specific for cardiac troponin-I, to form a particle/cardiac troponin-I/conjugate sandwich. Unbound conjugate is removed by magnetic separation and washing. After separation and washing, the particle/cardiac troponin-I/conjugate sandwich is transferred to the cuvette where the sandwich bound ALP triggers an amplification cascade.* ALP dephosphorylates synthetic flavin adenine dinucleotide phosphate (FADP) to produce FAD. FAD binds to apo D-amino acid oxidase and converts it to active holo D-amino acid oxidase. Each molecule of holo D-amino acid oxidase then produces multiple molecules of hydrogen peroxide (H_2O_2) which, in the presence of horseradish peroxidase (HRP), convert 3,5-dichloro-2-hydroxybenzenesulfonic acid (DCHBS) and 4-aminoantipyrine (4-AAP) to a colored product that absorbs at 510 nm. The color change measured is directly proportional to the concentration of cardiac troponin-I present in the patient sample.

* Technology licensed from London Biotechnology, Ltd., London, U.K.

$$cTnI + CrO_2\text{-}Ab + Fab'\text{-}ALP \longrightarrow CrO_2\text{-}Ab\text{-}cTnI\text{-}Fab'\text{-}ALP + CrO_2\text{-}Ab + Fab'\text{-}ALP$$

$$CrO_2\text{-}Ab\text{-}cTnI\text{-}Fab'\text{-}ALP + CrO_2\text{-}Ab + Fab'\text{-}ALP \xrightarrow{\text{Wash}} CrO_2\text{-}Ab\text{-}cTnI\text{-}Fab'\text{-}ALP + CrO_2\text{-}Ab$$

(transferred to cuvette)

$$FADP \xrightarrow{CrO_2\text{-}Ab\text{-}cTnI\text{-}Fab'\text{-}ALP} FAD + Pi$$

$$\text{apo D-amino acid oxidase} \xrightarrow{FAD} \text{holo D-amino acid oxidase}$$

$$D\text{-proline} + O_2 \xrightarrow{\text{Holo D-amino acid oxidase}} H_2O_2$$

$$H_2O_2 + DCHBS + 4\text{-}AAP \xrightarrow{HRP} \text{Color (absorbs at 510 nm)}$$

cTnI = cardiac troponin-I

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3. SPECIMEN REQUIREMENTS

3.1 Patient Preparation

Component	Special Notations
Fasting/Special Diets	N/A
Specimen Collection and/or Timing	Use normal procedures for blood collection. Collect anytime requested by physician. Serial samples are generally taken at 6-8 hour intervals over the first 48 hours after the onset of chest pain in patients suspected of suffering myocardial infarction.
Special Collection Procedures	N/A
Other	N/A

3.2 Specimen Type & Handling

Criteria		
Type -Preferred	Plasma (Heparin)	
-Other Acceptable	Serum	
Collection Container	Plasma: Green top plasma separator tube Serum: Red top tube, Serum separator tube (SST)	
Volume - Optimum	1.0 mL	
- Minimum	0.5 mL	
Transport Container and Temperature	Collection container or Plastic vial at room temperature	
Stability & Storage Requirements	Room Temperature:	(20-25°C) 8 hours
	Refrigerated:	(2-8°C) 2 days
	Frozen:	(-20°C or colder) 1 month
Timing Considerations	N/A	
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 redraw. Credit the test with the appropriate LIS English text code explanation of HMT (Specimen markedly hemolyzed)	
Other Considerations	Allow to clot completely prior to centrifugation.	

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4. REAGENTS

Refer to the Material Safety Data Sheet (MSDS) supplied with the reagents for complete safety hazards. Refer to the section in this procedure covering "SAFETY" for additional information.

4.1 Reagent Summary

Reagents	Supplier & Catalog Number
Cardiac Troponin-I	Siemens, Flex® reagent cartridge, Cat. No. RF421C

4.2 Reagent Preparation and Storage

NOTES: Date and initial all reagents upon opening. Each container must be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech, (6) any special storage instructions; check for visible signs of degradation.
Refer to the Material Safety Data Sheet (MSDS) for a complete description of hazards. If a specific hazard is present, it will be noted in this procedure when the hazard is first encountered in a procedural step.

Irritant. Contains mixture of 5-chloro-2-mtheyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1)
May cause sensitization by skin contact.

Reagent	**Cardiac Troponin-I**
Container	Reagent cartridge
Storage	Store at 2-8° C
Stability	• Reagent is stable until expiration date stamped on the reagent cartridges. • Sealed or unhydrated cartridge wells on the instrument are stable for 30 days. • Once wells 1 – 8 have been entered by the instrument, they are stable for 3 days.
Preparation	Hydrating, dilution and mixing are automatically performed by the instrument.

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
Cardiac Troponin I Calibrator	Siemens Dimension®, Cat. No. RC421C

5.2 Calibrator Preparation and Storage

NOTE: Date and initial all calibrators upon opening. Each container must be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech (6) any special storage instructions; check for visible signs of degradation.

Irritant. Contains mixture of 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1).
May cause sensitization by skin contact.
Avoid contact with skin.

Calibrator	Cardiac Troponin I Calibrator
Preparation	Before use, thaw and equilibrate at room temperature for one hour (not to exceed two hours). Mix the contents of the vial by inverting gently ten times. Do not use glass pipettes when transferring calibrators to sample cups.
Storage/Stability	• Store frozen at -25 to -15°C • **Unopened frozen vials** are stable until the expiration date printed on the label. • **Unopened thawed vials** are stable for 5 days when stored at 2-8°C. • **Opened vials (thawed)** are stable for 24 hours when thawed, recapped and stored at 2-8°C.

5.3 Calibration Parameter

Criteria	**Special Notations**
Reference Material	Cardiac Troponin-I Calibrator
Assay Range	0.04 – 40.0 ng/mL
Suggested calibration level	See reagent package insert for lot specific assigned values in ng/mL
Frequency	• Every new reagent cartridge lot. • Every 60 days for any one lot. • When major maintenance is performed on the analyzer. • When control data indicates a significant shift in assay.
Calibration Scheme	Levels 1, 2 n = 4 Level 3 n = 3 Level 4, 5 n = 2
Assigned Coefficients	C_0 - 989.0 C_1 8439.0 C_2 - 2.9 C_3 101.0 C_4 0.5

5.4 Calibration Procedure

1. From Operating Menu press F5:Process Control press F1: Calibration Enter Password press F2: SETUP and RUN
2. Select the test method to be calibrated - if lot number is incorrect Press F1: Other Lot
3. Enter all information on screen
4. Press F8: QC yes/no to change to yes
5. Press F4: Assign cups If additional methods need to be calibrated, select the method.
6. Press F7: Load/run
7. Load cups into assigned position
8. Press F4: RUN

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
Liquichek Cardiac Markers Plus Control, Levels 1, 2 and 3	Bio-Rad Laboratories Cat # 181, 182 and 183

6.2 Control Preparation and Storage

NOTE: Date and initial all controls upon opening. Each container should be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech, and (6) any special storage instructions; check for visible signs of degradation.

Control	Liquichek Cardiac Markers Plus Control, Levels 1, 2 and 3
Preparation	Allow the frozen control to thaw at room temperature (18-25°C) 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	Once the product is thawed and opened, Troponin I will be stable for 10 days at 2-8°C. Unopened controls are stable until the expiration date at -20 to -70°C.

6.3 Frequency

Analyze all levels of QC material after every calibration and each day of testing.

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

6.4 Tolerance Limits

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

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Quest Diagnostics
Site: Germantown Emergency Center
Title: **Cardiac Troponin-I by Dimension® Xpand Chemistry Analyzer**

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Step	Action
	Control Program.
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 Review Patient Data

Technologist must review each result with error messages. Refer to the Dimension Xpand® system manual "Error messages" section for troubleshooting. Check for unusual patterns, trends, or distributions in patient results (such as an unusually high percentage of abnormal results). Resolve any problems noted before issuing patient reports.

6.6 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.

6.7 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 Xpand® System

7.2 Equipment

- Refrigerator capable of sustaining 2–8°C.
- Freezer capable of sustaining range not to exceed -15 to -25°C.
- Centrifuge

7.3 Supplies

- Plastic serum tubes and serum cups
- Purified water (Millipore® or equivalent)
- Calibrated pipettes and disposable tips
- Reaction Vessels, Cat. No. RXV1A
- Chemistry Wash, Cat. No. RD701
- Reagent Probe Cleaner, Cat. No. RD702
- Sample Probe Cleaner, Cat. No. RD703

8. PROCEDURE

CTNI Flex® reagent cartridge Cat. No. RF421C is required to perform this test.

Troponin-I is performed on the Dimension Xpand® 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.

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.

8.1	Instrument Set-Up Protocol
1.	For instrument set up and operation: Refer to Startup and Maintenance, Siemens Dimension® Xpand procedure.
2.	Check reagent inventory
3.	Sampling, reagent delivery, mixing, processing, and printing of results are automatically performed by the Dimension® Xpand system. For details of the automated parameters, see below under "Test conditions."

8.2	Specimen/Reagent Preparation
1.	Centrifuge the specimens.

8.2	Specimen/Reagent Preparation
2.	Specimens are placed in Dimension® Xpand segments for analysis by the instrument. Refer to the Sample Processing, Siemens Dimension® Xpand procedure. The sample container (if not a primary tube) must contain sufficient quantity to accommodate the sample volume plus 50 µL of dead volume. Precise container filling is not required.

8.3	Specimen Testing
1.	For QC placement and frequency, refer to the Dimension® Xpand QC Schedule in the Laboratory QC Program.
2.	Follow the instructions, outlined in the Dimension® Xpand Operators 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® Xpand system manual "Error messages" section for troubleshooting.
4.	Follow protocol in Section 10.5 "Repeat criteria and resulting" for samples with results above or below the Analytical Measurement Range (AMR). Repeat critical values and document according to Critical Values procedure. 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 Size:	50 µL	
Antibody-CrO_2:	25 µL	
Antibody-ALP:	40 µL	
Incubating Temp.:	42° C	
Incubation Period:	4.0 minutes	
Cuvette	**Reaction**	**Blanking**
Transfer Volume:	65 µL	0 µL
FADP Reagent Volume:	24 µL	24 µL
APO Reagent Volume:	24 µL	24 µL
Diluent Volume:	267 µL	332 µL
Temperature:	37.0 ° C	N/A
Reaction Time:	5.4 minutes	N/A
Wavelength:	510 and 700 nm	N/A
Type of Measurement:	Bichromatic rate	N/A

9. CALCULATIONS

The instrument automatically calculates and prints the concentration of Troponin-I in ng/mL.

10. REPORTING RESULTS AND REPEAT CRITERIA

10.1 Interpretation of Data

None required

10.2 Rounding

No rounding is necessary. Instrument reports results to two decimal points.

10.3 Units of Measure

ng/mL

10.4 Clinically Reportable Range (CRR)

0.04 - 200.00 ng/mL

10.5 Repeat Criteria and Resulting

Any samples immediately following a sample that reached upper AMR and are above the upper normal limit will be repeated along with a low level control to ensure no carryover occurred.

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

Values requiring **manual dilution** must be repeated.

IF the result is …	THEN…
≤ 0.04 ng/mL	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: <0.04 ng/mL
≥ 40.00 ng/mL	**On Board Automated Dilution:** Results ≥ 40.00 ng/mL will automatically have repeat testing performed into the instrument using dilution factor of 2.5. No multiplication is necessary.
> 100.00 ng/mL	**Manual Dilution:** Using the primary tube, make the smallest dilution possible to bring the raw data within the AMR. Maximum allowable dilution: x 5 **Diluent:** Purified water. Enter dilution factor as a whole number on the "Enter Sample Data" screen. For values requiring manual dilution, report the assay with code of –REP
>200.00 ng/mL	If the recommended dilution does not give results within the clinically reportable range, report as: ">200.00 ng/mL-REP" Bring to the attention of your supervisor prior to releasing result.

.

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

11. EXPECTED VALUES

11.1 Reference Ranges

0.00 – 0.10 ng/mL

11.2 Critical Values

≥ 0.6 ng/mL

Treatment of **Subsequent critical values** for Troponin-I:
Only the first critical value must be called. Subsequent critical values for troponin must be documented by appending the code **TROPC** to the result. This code translates to "Laboratory value indicates a critical value previously reported."

11.3 Priority 3 Limit(s)

None established

12. CLINICAL SIGNIFICANCE

Troponin-I is the contractile regulatory protein complex of striated muscle. It is found periodically along the thin filament of the myofibrils, in conjunction with the protein tropomyosin. The troponin complex consists of three distinct polypeptide components: troponin-C (the calcium binding element), troponin-I (the actinomyosin ATPase inhibitory element), and troponin-T (the tropomyosin binding element). The complex serves to regulate the calcium-dependent interaction of myosin and actin and thus plays an integral role in muscle contraction.

Troponin-I exists in three distinct molecular forms which correspond to specific isotypes found in fast-twitch skeletal muscle, slow-twitch skeletal muscle, and heart, respectively. The skeletal isotypes are similar in molecular size, approximately 20,000 daltons, but exhibit amino acid sequence heterogeneity of approximately 40%. The cardiac isotype also exhibits about a 40% sequence heterogeneity with respect to the skeletal isotypes, but also has an additional 31 residues at the amino terminus, resulting in a molecular weight of about 24,000 daltons.

Several reports in the literature have indicated that cardiac troponin-I is released into blood within hours of the onset of symptoms of myocardial infarction and that it remains elevated for several days post-infarction. The cumulative data from these reports indicate that troponin-I levels become abnormal 4-8 hours following onset of chest pain, peak at 12-16 hours, and remain elevated for 5-9 days following an infarction. Based upon these studies it appears that troponin-I is elevated over a time period which covers the diagnostic window of

both CKMB and LD. Recent clinical studies also suggest an improved cardiac specificity for troponin-I compared to CKMB for detection of myocardial injury in the presence of skeletal muscle injury.

Measurement of cardiac troponin-I levels provide sensitive and specific determination of myocardial injury over a wide diagnostic window. Elevations in cardiac troponin-I levels have been observed across a spectrum of acute coronary syndromes including Q-wave MI, non-Q-wave MI and unstable angina. A significantly higher incidence of mortality has been observed in patients with non-Q-wave MI and unstable angina who have detectable levels of cardiac troponin-I. This suggests that cardiac troponin-I provides a means for risk stratification of these individuals.

The CTNI method for the Dimension® clinical chemistry system with the heterogeneous immunoassay module is an *in vitro* diagnostic test intended to quantitatively measure cardiac troponin-I levels in serum and heparinized plasma to aid in the diagnosis of myocardial infarction and in the risk stratification of patients with acute coronary syndromes with respect to their relative risk of mortality.

Interpretation of Results: Clinical studies indicate that levels of cardiac troponin-I are a useful indicator of myocardial injury for a range of acute coronary syndromes including unstable angina, non Q-wave and Q-wave myocardial infarction.

Risk Stratification: Statistically significant increases in mortality have been observed as a function of increasing levels of cardiac troponin-I. In patients with acute coronary syndromes such as unstable angina or non-Q-wave myocardial infarction, cardiac troponin-I levels provide useful prognostic information and aid in early detection of such patients with an increased risk of death. In a clinical study performed using the Dimension® cardiac troponin-I method, unstable angina patients whose cardiac troponin-I levels were at least 0.1 ng/mL [µg/L] within the first 24 hours were at higher risk of death or MI at 48 hours and 14 days than patients whose cardiac troponin-I levels were below 0.1 ng/mL [µg/L].

Diagnosis of AMI

Interpretation of Results: The temporal evaluation of cardiac troponin-I concentration is a useful tool in the diagnosis of a myocardial infarction. A sequential sampling protocol is recommended. Serial samples from a patient with a myocardial infarction taken at 6-8 hour intervals over the first 48 hours will result in the classic rise and fall in concentration observed with other markers of myocardial infarction such as CK-MB. Unlike CK-MB, cardiac troponin-I values generally remain elevated above the reference range for several (5-9) days. National Academy of Clinical Biochemists (NACB) and the World Health Organization (WHO) requires two of the following criteria for confirmation of AMI; ECG changes consistent with infarction, temporal changes in cardiac enzyme/marker levels, chest discomfort of significant duration (≥ 20 minutes).

Other conditions which can lead to myocardial injury, such as cardiac contusion and myocarditis, have the potential to cause elevations in the circulation concentrations of proteins found in the myocardium, including cardiac troponin-I. Factors such as these should be considered when interpreting results.

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 Xpand Operator's Guide.

A system malfunction may exist if the following 5-test precision is observed:

Concentration	S.D.
2.0 ng/mL	> 0.20 ng/mL
25.0 ng/mL	> 1.50 ng/mL

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

0.04 – 40.00 ng/mL

14.2 Precision

Material	Mean ng/mL	Standard Deviation (%CV)	
		Within-run	Total
MAS Tru-Liquid Control			
Level 1	0.35	0.01 (2.7)	0.03 (7.7)
Level 2	5.28	0.05 (1.0)	0.22 (4.2)
Level 3	14.52	0.14 (1.0)	0.71 (4.9)
Serum Pool			
Level 1	0.08	0.01 (7.3)	0.01 (15.1)
Level 2	0.16	0.01 (4.0)	0.01 (9.2)
Level 3	0.47	0.01 (2.9)	0.03 (6.2)
Level 4	1.44	0.04 (2.6)	0.07 (5.2)
Level 5	27.71	0.53 (1.9)	0.99 (3.6)
Level 6	40.05	0.75 (1.9)	1.81 (4.5)

14.3 Interfering Substances

Patient samples may contain heterophile antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay has been designed to minimize interference from heterophile antibodies. Complete elimination of the interference cannot be guaranteed. A test result that is inconsistent with the clinical picture and patient history should be interpreted with caution.

14.4 Clinical Sensitivity/Specificity/Predictive Values

Not available.

15. SAFETY

The employee has direct responsibility to avoid injury and illness at work. Nearly all harmful exposures to infectious substances and chemicals, and other injuries, can be avoided with effective training and consistent safe work practices.

Become familiar with the Environmental Health and Safety (EHS) Manual to learn the requirements on working safely and protecting the environment from harm. Although lab work typically focuses on the hazards of working with specimens and chemicals, we must also control other important hazards.

- Slips, trips, and falls cause many serious injuries. Please ensure that spills are cleaned quickly (to avoid slippery floors) and that you can see and avoid obstacles in your path.
- Ergonomic injuries result from performing tasks with too much repetition, force, or awkward position. Ergonomic injuries include strains and back injuries. Learn about ergonomic hazards and how to prevent this type of injury.
- Scratches, lacerations, and needlesticks can result in serious health consequences. Attempt to find ways to eliminate your risk when working with sharp materials.

Report all accidents and injuries immediately to your supervisor or the business unit Environmental Health and Safety Manager or Specialist.

16. RELATED DOCUMENTS

1. Dimension Xpand® Clinical Chemistry System Operator's Manual
2. Calibration / Verification Siemens Dimension® Xpand procedure
3. Dimension Xpand® Cal Accept Guidelines
4. Dimension Xpand® Calibration summary
5. Sample Processing, Siemens Dimension® Xpand procedure
6. Start up and Maintenance, Siemens Dimension® Xpand procedure
7. Laboratory Quality Control Program
8. QC Schedule for Siemens Dimension Xpand®
9. Laboratory Safety Manual
10. Material Safety Data Sheets (MSDS)
11. Siemens Dimension Xpand® Limits Chart (AG.F143)
12. Quest Diagnostics Records Management Procedure
13. Dimension Xpand® System Error Messages Chart
14. Centrifuge Use, Maintenance and Functions Checks (Lab policy)
15. Hemolysis, Icteria and Lipemia Interference (Lab policy)
16. Repeat Testing Requirements (Lab policy)
17. Critical Values (Lab policy)
18. Current Allowable Total Error Specifications at http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls
19. Current package insert CTNI Flex® Reagent Cartridge RF421C

17. REFERENCES

1. Package Insert, CTNI Flex® Reagent Cartridge RF421C, Siemens Healthcare Diagnostics Inc., 03/12/2009.
2. Package insert, Cardiac Troponin-I Calibrator RC421C, Siemens Healthcare Diagnostics Inc., 10/2014.
3. Package insert, Liquichek Cardiac Markers Plus Control Levels 1, 2 & 3. Bio-Rad Laboratories, 11/2011.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
			Supersedes SOP C072.001		
000	7/15/11	6.7	Add use of published TEA for acceptability criteria	L Barrett	N Cacciabeve
000	7/15/11	10.5	Change repeat criteria to manual dilutions only	R SanLuis	N Cacciabeve
000	7/15/11	11.2	Requirement for subsequent critical values and interpretation of code revised	L Barrett	N Cacciabeve
000	7/15/11	15	Update to approved format	L Barrett	N Cacciabeve
001	2/8/12	5.3	Changed calibration level statement	A. Chini	J Buss
001	2/8/12	6.1 & 6.2	Updated QC information	A. Chini	J Buss
001	2/8/12	10.2	Correct rounding to 2 decimals	A. Chini	J Buss
001	2/8/12	10.5	Remove QNSR code	L Barrett	J Buss
001	2/8/12	10.5	Add repeat criteria for possible carryover	J Buss	J Buss
001	2/8/12	17	Updated References	A. Chini	J Buss
002	4/2/15		Update owner	L Barrett	R SanLuis
002	4/2/15	1, 7.1	Add analyzer name	L Barrett	R SanLuis
002	4/2/15	5.2	Change in frozen storage temperature	L Barrett	R SanLuis
002	4/2/15	6.2	Update stability to 10 days	L Barrett	R SanLuis
002	4/2/15	6.4, 6.6	Replace LIS with Unity Real Time	L Barrett	R SanLuis
002	4/2/15	7.2	Change freezer requirements	L Barrett	R SanLuis
002	4/2/15	8.2	Remove Lynx, specify Xpand process	L Barrett	R SanLuis
002	4/2/15	Footer	Version # leading zero's dropped due to new EDCS in use as of 10/7/13	L Barrett	R SanLuis

19. ADDENDA

None

Approved draft for training

Technical SOP

Title	**Creatine Kinase by Dimension® Xpand Chemistry Analyzer**
Prepared by	Ashkan Chini Date: 3/30/2011
Owner	Robert SanLuis Date: 6/20/2013

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

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1. TEST INFORMATION

Assay	Method/Instrument	Local Code
Creatine Kinase	Dimension® Xpand Chemistry Analyzer	CPK

Synonyms/Abbreviations
CK, CPK, CKI

Department
Chemistry

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2. ANALYTICAL PRINCIPLE

CK catalyzes the transphosphorylation of phosphate from creatine phosphate to adenosine-diphosphate (ADP) producing adenosine-triphosphate (ATP). Hexokinase (HK) phosphorylates glucose from the ATP to phosphorylate glucose. 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.

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

$$\text{ATP} + \text{Glucose} \xrightarrow[Mg^{++}]{\text{HK}} \text{ADP} + \text{Glucose-6-phosphate}$$

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

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	None
Other	N/A

3.2 Specimen Type & Handling

Criteria	
Type -Preferred	Plasma (Heparin)
-Other Acceptable	Serum
Collection Container	Plasma: Green top tube Serum: Red top tube, Serum separator tube (SST)
Volume - Optimum	1.0 mL
- Minimum	0.5 mL
Transport Container and Temperature	Collection tube or plastic vial at room temperature
Stability & Storage Requirements	Room Temperature: 2 hours
	Refrigerated: (2-8°C) 7 days
	Frozen: (-20°C or colder) 1 month
Timing Considerations	Serum 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.
Other Considerations	Allow to clot completely prior to centrifugation.

4. REAGENTS

Refer to the Material Safety Data Sheet (MSDS) supplied with the reagents for complete safety hazards. Refer to the section in this procedure covering "SAFETY" for additional information.

4.1 Reagent Summary

Reagents	Supplier & Catalog Number
Creatine Kinase	Siemens, Flex® reagent cartridge, Cat. No. DF38

4.2 Reagent Preparation and Storage

NOTES: Date and initial all reagents upon opening. Each container must be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech, (6) any special storage instructions; check for visible signs of degradation.
Refer to the Material Safety Data Sheet (MSDS) for a complete description of hazards. If a specific hazard is present, it will be noted in this procedure when the hazard is first encountered in a procedural step.

Quest Diagnostics
Site: Germantown Emergency Center
Title: **Creatine Kinase by Dimension® Xpand Chemistry Analyzer**

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Reagent	**Creatine Kinase**
Container	Reagent cartridge
Storage	Store at 2-8°C
Stability	• Reagent is stable until expiration date stamped on the reagent cartridges. • Sealed or unhydrated cartridge wells on the instrument are stable for 30 days. • Once wells 1 – 4 have been entered by the instrument, they are stable for 5 days. • Once wells 5 – 6 have been entered by the instrument, they are stable for 10 days.
Preparation	Reagents are supplied ready for use. No additional preparation is required.

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
CKI/MBI CAL	Siemens Dimension®, Cat. No. DC32

5.2 Calibrator Preparation and Storage

NOTE: Date and initial all calibrators upon opening. Each container must be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech (6) any special storage instructions; check for visible signs of degradation.

Calibrator	CKI/MBI CAL
Preparation	Thaw at room temperature for 30 – 45 minutes before use. Do not thaw in a water bath or water above 25°C. Before use, mix the contents of the vial by inverting gently ten times.
Storage/Stability	• Store frozen at -25 to -15°C • The unopened calibrator is stable until the expiration date printed on the label • Once thawed, assigned values are stable for 7 days when recapped immediately after use and stored at 2 - 8°C

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	CKI/MBI 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	Three levels in triplicate.
Assigned Coefficients	C_0 1.708 C_1 8.044

5.4 Calibration Procedure

1. From Operating Menu press F5:Process Control press F1: Calibration Enter Password press F2: SETUP and RUN
2. Select the test method to be calibrated - if lot number is incorrect Press F1: Other Lot
3. Enter all information on screen
4. Press F8: QC yes/no to change to yes
5. Press F4: Assign cups If additional methods need to be calibrated, select the method.
6. Press F7: Load/run
7. Load cups into assigned position
8. Press F4: RUN

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
Liquichek™ Unassayed Chemistry Controls Levels 1 & 2	Bio-Rad Laboratories Cat. No. 691 & 692

6.2 Control Preparation and Storage

NOTE: Date and initial all controls upon opening. Each container should be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech, and (6) any special storage instructions; check for visible signs of degradation.

Control	Liquichek Unassayed Chemistry Controls Levels 1 & 2
Preparation	Allow the frozen control to stand at room temperature (18-25°C) 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	Open thawed controls are stable for 15 days at 2-8°C. Unopened controls are stable until the expiration date at -20 to -70°C.

6.3 Frequency

Analyze all levels of QC material after every calibration and each day of testing

Refer to the Dimension Xpand® QC Schedule in the Laboratory policy Quality Control Program and in the Dimension X-pand® Quick Reference Guide.

6.4 Tolerance Limits

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.
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 Review Patient Data

Technologist must review each result with error messages. Refer to the Dimension Xpand® system manual "Error messages" section for troubleshooting. Check for unusual patterns, trends, or distributions in patient results (such as an unusually high percentage of abnormal results). Resolve any problems noted before issuing patient reports.

6.6 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.

6.7 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 Xpand® System

7.2 Equipment

- Refrigerator capable of sustaining 2–8°C.
- Freezer capable of sustaining range not to exceed -15 to -25°C.
- Centrifuge

7.3 Supplies

- Plastic serum tubes and serum cups
- Purified water (Millipore® or equivalent)
- Calibrated pipettes and disposable tips

8. PROCEDURE

CKI Flex® reagent cartridge Cat. No. DF38 is required to perform this test.

Creatine Kinase is performed on the Dimension Xpand® 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.

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.

8.1	Instrument Set-Up Protocol
1.	For instrument set up and operation: Refer to Startup and Maintenance, Siemens Dimension® Xpand procedure.
2.	Check reagent inventory
3.	Sampling, reagent delivery, mixing, processing, and printing of results are automatically performed by the Dimension® Xpand system. For details of the automated parameters, see below under “Test conditions.”

8.2	Specimen/Reagent Preparation
1.	Centrifuge the specimens.
2.	Specimens are placed in Dimension® Xpand segments for analysis by the instrument. Refer to the Sample Processing, Siemens Dimension® Xpand procedure. The sample container (if not a primary tube) must contain sufficient quantity to accommodate the sample volume plus 50 µL of dead volume. Precise container filling is not required.

8.3	Specimen Testing
1.	For QC placement and frequency, refer to the Dimension® Xpand QC Schedule in the Laboratory QC Program.
2.	Follow the instructions, outlined in the Dimension® Xpand Operators 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® Xpand system manual “Error messages” section for troubleshooting.
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 Size:	14 µL
Reagent 1 Volume:	112 µL
Reagent 2 Volume:	55 µL
Reaction Time:	8.7 minutes
Temperature:	37° C
Wavelength:	340 and 540 nm
Type of Measurement:	Bichromatic rate

9. CALCULATIONS

The instrument automatically calculates and prints 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 – 20,000 U/L

10.5 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 within the AMR or CRR may be reported without repeat. Values that fall outside these 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. No multiplication is necessary.
>7,000 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 20 **Diluent**: Reagent Grade Water Enter dilution factor as a whole number on the "Enter Sample Data" screen.

>20,000 U/L	If the recommended dilution does not give results within the clinically reportable range, report as: ">20,000 U/L-REP" Bring to the attention of your supervisor prior to releasing result.

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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:		
0– 90 days	43-474	29-303
3 – 12 months	27-242	25-172
13 months – 23 months	25-177	28-162
2 – 10 years	25-177	31-152
11 – 14 years	31-172	31-152
15 – 18 years	28-142	34-147

11.2 Critical Values

None established

11.3 Priority 3 Limit(s)

None established

12. CLINICAL SIGNIFICANCE

Measurements of Creatine Kinase are used in the diagnosis and treatment of myocardial infarction and muscle disease, such as progressive Duchenne-type muscular dystrophy. Creatine Kinase (CK) is an enzyme that is found primarily in skeletal muscle, cardiac muscle and brain tissue. Elevated levels of CK are associated with myocardial infarction and various muscle disorders. In myocardial infarction, peak CK levels occur 24 to 36 hours after onset of chest pain and depending on the extent of damage can reach more than 10 times normal levels. In Reye's Syndrome, up to a 70-fold increase in CK activity may be seen due to severe encephalopathy.

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 Xpand Operator's Guide.

A system malfunction may exist if the following 5-test precision is observed:

Concentration	S.D.
150 U/L	> 7 U/L
800 U/L	> 16 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)	
		Within-run	Total
Serum			
Serum Pool 1	46	0.7	1.3
Serum Pool 2	166	1.4	3.5
Multiqual®			
Level 1	108	1.1	3.5
Level 3	788	3.3	13.4

14.3 Interfering Substances

HIL Interference:
The CKI was evaluated for interference according to CLSI/NCCLS EP7-A2. Bias is 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	Test Concentration SI Units	CKI Concentration U/L	Bias %
Hemoglobin (hemolysate)	100 mg/dL	200	<10
Bilirubin	80 mg/dL	200	<10
Lipemia (Intralipid®)	3000 mg/dL	200	<10

14.4 Clinical Sensitivity/Specificity/Predictive Values

Not available.

15. SAFETY

The employee has direct responsibility to avoid injury and illness at work. Nearly all harmful exposures to infectious substances and chemicals, and other injuries, can be avoided with effective training and consistent safe work practices.

Become familiar with the Environmental Health and Safety (EHS) Manual to learn the requirements on working safely and protecting the environment from harm. Although lab work typically focuses on the hazards of working with specimens and chemicals, we must also control other important hazards.

- Slips, trips, and falls cause many serious injuries. Please ensure that spills are cleaned quickly (to avoid slippery floors) and that you can see and avoid obstacles in your path.
- Ergonomic injuries result from performing tasks with too much repetition, force, or awkward position. Ergonomic injuries include strains and back injuries. Learn about ergonomic hazards and how to prevent this type of injury.
- Scratches, lacerations, and needlesticks can result in serious health consequences. Attempt to find ways to eliminate your risk when working with sharp materials.

Report all accidents and injuries immediately to your supervisor or the business unit Environmental Health and Safety Manager or Specialist.

16. RELATED DOCUMENTS

1. Dimension Xpand® Clinical Chemistry System Operator's Manual
2. Calibration / Verification Siemens Dimension® Xpand procedure
3. Dimension Xpand® Cal Accept Guidelines
4. Dimension Xpand® Calibration summary
5. Sample Processing, Siemens Dimension® Xpand procedure
6. Start up and Maintenance, Siemens Dimension® Xpand procedure
7. Laboratory Quality Control Program
8. QC Schedule for Siemens Dimension Xpand®
9. Laboratory Safety Manual
10. Material Safety Data Sheets (MSDS)
11. Siemens Dimension Xpand® Limits Chart
12. Quest Diagnostics Records Management Procedure
13. Dimension Xpand® System Error Messages Chart
14. Centrifuge Use, Maintenance and Functions Checks (Lab policy)
15. Hemolysis, Icteria and Lipemia Interference (Lab policy)
16. Repeat Testing Requirements (Lab policy)
17. Current Allowable Total Error Specifications at http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls
18. Current package insert CKI Flex® Reagent Cartridge DF38

17. REFERENCES

1. Ghoshal, 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 DF38, Siemens Healthcare Diagnostics Inc., 10/31/2012.
3. Package insert, CKI/MBI CAL DC32, Siemens Healthcare Diagnostics Inc., 07/2014.
4. Package insert, Liquichek Unassayed Serum Chemistry Controls, Bio-Rad Laboratories, 12/2011.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
			Supersedes SOP C096.001		
000	5/31/11	10.4	Change CRR upper limit	L. Barrett	J. Buss
000	5/31/11	10.5	Correct all values to match CRR & AMR	L. Barrett	J. Buss
001	6/13/12	10.4	Correct CRR lower limit	J. Buss	J. Buss
002	6/20/13		Update owner	L Barrett	R SanLuis
002	6/20/13	1, 7.1	Add analyzer name	L Barrett	R SanLuis
002	6/20/13	4	Remove enzyme diluent (not used)	A Chini	R SanLuis
002	6/20/13	5	Corrected calibrator, preparation, storage	A Chini	R SanLuis
002	6/20/13	6.4	Delete QC ranges stored in instrument	L Barrett	R SanLuis
002	6/20/13	6.7	Add use of TEA for lot to lot runs	L Barrett	R SanLuis
002	6/20/13	8.2	Remove Lynx, specify Xpand process	L Barrett	R SanLuis
002	6/20/13	10.5	Corrected diluent to reagent grade water	A Chini	R SanLuis
002	6/20/13	16	Update document titles	L Barrett	R SanLuis
002	6/20/13	17	Add CKI/MBI CAL, Remove CK Verifier and Enzyme Diluent	A Chini	R SanLuis
003	4/2/15	5.2	Change in frozen storage temperature and thawed stability	L Barrett	R SanLuis
003	4/2/15	6.4, 6.6	Replace LIS with Unity Real Time	L Barrett	R SanLuis
003	4/2/15	7.2	Change freezer requirements	L Barrett	R SanLuis
003	4/2/15	Footer	Version # leading zero's dropped due to new EDCS in use as of 10/7/13	L Barrett	R SanLuis

19. ADDENDA

None