

TRAINING UPDATE

Lab Location: GEC
Department: Core

Date Distributed: 10/6/2016
Due Date: 10/19/2016
Implementation: 10/19/2016

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:

**Creatinine by Dimension® Xpand Chemistry Analyzer
GEC.C238 v1**

Description of change(s):

Section	Reason
4,5,6	Remove individual section labeling instructions and add general one
9.3	Change eGFR calculation frequency to once per 12 hours (calculated by the LIS, this change is already implemented)
10.5	Move patient review from section 6
15	Update to new standard wording, add reagent warning from section 4

This revised SOP will be implemented on October 19, 2016

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

Technical SOP

Title	Creatinine by Dimension® Xpand Chemistry Analyzer	
Prepared by	Ashkan Chini	Date: 10/8/2015
Owner	Robert SanLuis	Date: 10/8/2015

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

Review		
Print Name	Signature	Date

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1. TEST INFORMATION

Assay	Method/Instrument	Order Code
Creatinine, Serum/Plasma	Dimension® Xpand Chemistry Analyzer	CREAT

Synonyms/Abbreviations
Serum/Plasma creatinine

Department
Chemistry

2. ANALYTICAL PRINCIPLE

The creatinine method employs a modification of the kinetic Jaffe reaction reported by Larsen. This method has been reported to be less susceptible than conventional methods to interference from non-creatinine, Jaffe-positive compounds. Creatinine is generally regarded as the most useful endogenous substance to measure for the assessment of kidney function.

In the presence of a strong base such as NaOH, picrate reacts with creatinine to form a red chromophore. The rate of increasing absorbance at 510 nm due to the formation of this chromophore is directly proportional to the creatinine concentration in the sample and is measured using a bichromatic (510, 600 nm) rate technique. Bilirubin is oxidized by potassium ferricyanide to prevent interference.



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	Serum/ Plasma: Plastic vial or spun barrier tube at room temperature
Stability & Storage Requirements	Room Temperature: Serum/Plasma: 24 hours
	Refrigerated: (2-8°C) Serum/Plasma: 7 days
	Frozen: (-20°C or colder) Serum/Plasma: 3 months
Timing Considerations	N/A

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Criteria	
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.

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.

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
Creatinine (CRE2)	Siemens, Flex® reagent cartridge, Cat. No. DF33B

4.2 Reagent Preparation and Storage

Reagent	Creatinine
Container	Reagent cartridge
Storage	Store at 2-8° C
Stability	<ul style="list-style-type: none"> 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 – 6 have been entered by the instrument, they are stable for 3 days.
Preparation	All reagents are liquid and ready to use.

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5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
CHEM I Calibrator	Siemens Dimension®, Cat. No. DC18C

5.2 Calibrator Preparation and Storage

Calibrator	CHEM I Calibrator
Preparation	<ul style="list-style-type: none"> Remove vials from refrigerator and proceed directly to next step. Remove stopper and add 2.00 ± 0.01 ml Purified Water Diluent or Millipore water. The water should be at room temperature (22 - 28° C). Replace stopper, and let stand for 5 minutes. Do not invert. Swirl vials gently for 30 seconds, and then gently invert 10 times. Let vials stand for 10 minutes, and then gently invert 10 times. Let vial stand for 15 minutes. Then invert 10 times and swirl gently. Use immediately or refrigerate at 2-8°C for future use. Prior to use, invert 10 times and swirl gently.
Storage/Stability	<ul style="list-style-type: none"> Store at 2-8°C. The unopened reagents are stable until the expiration date printed on the label. Assigned values are stable for 24 hours after reconstitution when stoppered and stored at 2-8°C.

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	CHEM I Calibrator
Assay Range	0.15 – 20.00 mg/dL
Calibration levels	See reagent package insert for lot specific assigned values in mg/dL
Frequency	<ul style="list-style-type: none"> 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 - 0.3866 C ₁ 0.0823
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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 Control Levels 1 and 2	Bio-Rad Laboratories Cat. No. 691 and 692

6.2 Control Preparation and Storage

Control	Liquichek Unassayed Chemistry Control Levels 1 and 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 and unthawed 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 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 <ul style="list-style-type: none"> 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: <ul style="list-style-type: none"> 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 <u>reanalyzed according to the Laboratory QC Program</u>. 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.

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Step	Action
4	Review of QC <ul style="list-style-type: none">• 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 Xpand® System

7.2 Equipment

- Refrigerator capable of sustaining 2–8°C.

- Freezer capable of sustaining range not to exceed -20 to -70°C.
- Centrifuge

7.3 Supplies

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

8. PROCEDURE

CRE2 Flex® reagent cartridge Cat. No. DF33B is required to perform this test.

Creatinine 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.

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.

8.3	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.

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 and prints the concentration of Creatinine in mg/dL. The LIS performs the following calculation:

9.1 Estimated Glomerular Filtration Rate (eGFR)

For non-black individuals:

$$186 \times (\text{Serum Creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times$$

For black individuals:

$$186 \times (\text{Serum Creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210)$$

Notes:

- eGFR is only reported on patients 18 years of age or older.
- eGFR is calculated once per **12** ~~24~~ hours.
- If the creatinine result is corrected after initial reporting, verify that eGFR has also been corrected

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

Creatinine: mg/dL

eGFR: mL/min/1.73m²

10.4 Clinically Reportable Range (CRR)

0.15 - 60.00 mg/dL

10.5 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.

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 policy 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...
< 0.15 mg/dL	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: < 0.15 mg/dL
≥ 20.00 mg/dL	On Board Automated Dilution: Results ≥ 20.00 mg/dL for serum/plasma will automatically have repeat testing performed into the instrument using dilution factor of 2. No multiplication is necessary.
> 40.00 mg/dL	Manual Dilution: Using the primary tube, make the smallest dilution possible to bring the raw data within the AMR. Maximum allowable dilution: x 3 Diluent: Purified water. Enter dilution factor as a whole number on the “Enter Sample Data” screen.
>60.00 mg/dL	If the recommended dilution does not give results within the clinically reportable range, report as: “>60.00 mg/dL-REP” Bring to the attention of your supervisor prior to releasing result.

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

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11. EXPECTED VALUES

11.1 Reference Ranges

Age	Female	Male
Adult (>18 years):	0.55 – 1.02 mg/dL	0.70 – 1.30 mg/dL
Pediatric:		
16 – 18 years	0.80 - 1.20	0.80 - 1.40
13 – 15 years	0.70 - 1.10	0.60 - 1.20
10 – 12 years	0.60 - 1.00	0.60 - 1.00
7 – 9 years	0.50 - 0.90	0.60 - 0.90
4 – 6 years	0.50 - 0.80	0.50 - 0.80
1 – 3 years	0.40 - 0.70	0.40 - 0.70
1 – 11 months	0.40 - 0.60	0.40 - 0.70
0 – 30 days	0.50 - 0.90	0.50 - 1.20

11.2 Critical Values

None established

11.3 Standard Required Messages

Each eGFR result has the following comment automatically reported by the LIS:

The eGFR equation utilized is the MDRD for Adults (patients 18 and older). The equation does not require weight as we utilize a normalized body surface area of 1.73m².

The table below shows population estimates for mean (average) estimated glomerular filtration (eGFR) by age. These means are derived from the NHANES III survey of over 10,000 individuals, demonstrating that eGFR varies across age groups and that kidney function tends to decline with age.

Age Years	Mean eGFR
18-29	116 mL/min/1.73m ²
30-39	107 mL/min/1.73m ²
40-49	99 mL/min/1.73m ²
50-59	93 mL/min/1.73m ²
60-69	85 mL/min/1.73m ²
70+	75 mL/min/1.73m ²

12. CLINICAL SIGNIFICANCE

The serum creatinine level is increased in renal disease. Measurement of serum creatinine is useful in evaluation of kidney glomerular function and in monitoring renal dialysis.

However, the serum level is not sensitive to early renal damage and responds more slowly than blood urea nitrogen (BUN) to hemodialysis during treatment of renal failure. The serum creatinine together with serum BUN is used to differentiate pre-renal, renal and post-renal (obstructive) azotemia since an elevated BUN with only slight to moderate elevation of creatinine suggests pre-renal or post-renal azotemia. Serum creatinine varies with the subject's age, body weight, and sex. It is sometimes low in subjects with relatively small muscle mass, cachectic patients, amputees, and in older persons. A serum creatinine level that would usually be considered normal does not rule out the presence of impaired renal function.

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.
1.00 mg/dL	> 0.10 mg/dL
18.60 mg/dL	> 0.50 mg /dL

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

0.15 – 20.00 mg/dL

14.2 Precision

Material	Mean mg/dL	Standard Deviation (% CV)	
		Within-run	Total
Serum Pool 1	1.32	0.04	0.04
Serum Pool 2	15.79	0.19	0.19

14.3 Interfering Substances

HIL Interference:

The CRE2 method was evaluated for interference from hemolysis, icterus and lipemia according to CLSI EP07-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	Test Concentration SI Units	CRE2 Conc mg/dL	Bias %
Hemoglobin (hemolysate)	500 mg/dL	1.5	<10
	1000 mg/dL	5.0	1.1
Bilirubin (conjugated)	20 mg/dL	1.5	<10
	40 mg/dL	5.0	-17.2
Bilirubin (unconjugated)	10 mg/dL	1.5	<10
	20 mg/dL	1.5	-20.2
	40 mg/dL	5	<10
Lipemia Intralipid®	1000 mg/dL	1.5	<10
	1500 mg/dL	1.5	11.3
	2000 mg/dL	5.0	<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.

CRE2 Flex® Reagent Cartridge is Corrosive. Contains sodium hydroxide. Causes severe burns and eye damage. Wear protective clothing, gloves and eye/face protection.

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. Safety Data Sheets (SDS)
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. Current Allowable Total Error Specifications at
http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls
18. Current package insert CRE2 Flex® Reagent Cartridge DF33B

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, CRE2 Flex® Reagent Cartridge DF33B, Siemens Healthcare Diagnostics Inc., 02/27/2014.
3. Package insert, CHEM I Calibrator DC18C, Siemens Healthcare Diagnostics Inc., 02/2014.
4. Package insert, Liquichek Unassayed Serum Chemistry Control, Bio-Rad Laboratories, 08/2014.
5. Quest Diagnostics SOP ID 300SA357, Creatinine, Serum and Fluid.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
0	9/26/16	4,5,6	Remove individual section labeling instructions and add general one	L Barrett	R SanLuis
0	9/26/16	9.3	Change eGFR calculation frequency to once per 12 hours	L Barrett	R SanLuis
0	9/26/16	10.5	Move patient review from section 6	L Barrett	R SanLuis
0	9/26/16	15	Update to new standard wording, add reagent warning from section 4	L Barrett	R SanLuis

19. ADDENDA

None