TRAINING UPDATE

Lab Location:	GEC	**Date Distributed:**	8/13/2015
Department:	Core	**Due Date:**	8/31/2015
		Implementation:	**9/1/2015**

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:

C-Reactive Protein by Dimension® Xpand Chemistry Analyzer GEC.C23v1

Description of change(s):

Most changes are minor.

Section	Reason
1, 7.1	Add analyzer name
3.2	Specify anticoagulant
4.2	Update hazard statement
5.3	Edit calibration levels statement
6.4, 6.6	Replace LIS with Unity Real Time
6.7	Add use of TEA for lot to lot runs
8.2	Remove Lynx
10.5	Remove use of code REP from dilutions, remove code QNSR
15	Update to standard wording
16	Update titles

This revised SOP will be implemented on September 1, 2015

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

Approved draft for training (version 1)

Technical SOP

Title	**C-Reactive Protein by Dimension® Xpand Chemistry Analyzer**
Prepared by	Ashkan Chini Date: 4/1/2011
Owner	Robert SanLuis Date: 4/1/2011

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**

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TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Local Code
C-Reactive Protein	Dimension® Xpand Chemistry Analyzer	CRP

Synonyms/Abbreviations
CRP

Department
Chemistry

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2. ANALYTICAL PRINCIPLE

The CRP method is based on a particle enhanced turbidimetric immunoassay (PETIA) technique. Synthetic particles coated with antibody to C-Reactive protein (AbPR) aggregate in the presence of C-Reactive protein in the sample. The increase in turbidity which accompanies aggregation is proportional to the C-Reactive protein concentration.

CRP + AbPR → Aggregate (Absorbs at 340 nm)

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 **-Other Acceptable**	Plasma (Lithium Heparin) Serum	
Collection Container	Plasma: Mint green top tube 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	
Stability & Storage Requirements	Room Temperature:	8 hours
	Refrigerated:	(4°C) 72 hours
	Frozen:	(-20°C or colder) 6 months
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	

Criteria	
	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
C-Reactive Protein	Siemens, Flex® reagent cartridge, Cat. No. DF37

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 5-chloro-2-methyl-3(2h)-isothiazolone mixture with 2-methyl-3(2h)- isothiazolone.
May cause an allergic skin reaction.
Wear protective gloves/protective clothing/eye protection/face protection.
Contaminated work clothing should not be allowed out of the workplace. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention

Reagent	**C-Reactive Protein**
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 – 6 have been entered by the instrument, they are stable for 3 days.

	• Once wells 7 – 8 have been entered by the instrument, they are stable for 30 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
C-Reactive Protein Calibrator	Siemens Dimension®, Cat. No. DC30

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	C-Reactive Protein Calibrator
Preparation	Allow to equilibrate to room temperature (22-28°C) and swirl to mix before use.
Storage/Stability	• Store at 2-8°C. • The unopened reagents are stable until the expiration date printed on the label. • Once opened, assigned values are stable for 24 hours when vials are stored securely capped at (2-8°C) between use.

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	C-Reactive Protein Calibrator
Assay Range	0.2 – 12.0 mg/dL
Suggested calibration level	See reagent package insert for lot specific assigned values in mg/dL
Frequency	• Every new reagent cartridge lot. • Every 2 months 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 – 5, n = 2.

Assigned Coefficients	C_0 –48.3 C_1 541.6 C_2 -3.4 C_3 28.0 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 Immunology Controls Levels 1, 2 & 3	Bio-Rad Laboratories Cat # 594, 595, & 596

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 Immunology Controls Levels 1, 2 & 3
Preparation	Frozen Control: Allow the control to stand at room temperature (18-25°C) until completely thawed. Thawed Control: Allow the control to reach room temperature. After the control reaches room temperature, swirl gently to ensure homogeneity. Promptly replace the stopper and return to 2 to 8°C storage after each use.
Storage/Stability	Open controls are stable for 30 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

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Step	Action
	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 -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

CRP Flex® reagent cartridge Cat. No. DF37 is required to perform this test.

C-Reactive Protein 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:	3 µL
Reagent 1 Volume:	284 µL
Reagent 2 Volume:	107 µL
Reagent 3 Volume:	20 µL
Diluent Volume:	66 µL
Temperature:	37°C
Wavelength:	340 and 700 nm
Type of Measurement:	Bichromatic rate

9. CALCULATIONS

The instrument automatically calculates and prints the concentration of CRP in mg/dL.

10. REPORTING RESULTS AND REPEAT CRITERIA

10.1 Interpretation of Data

None required

10.2 Rounding

No rounding is necessary. Instrument reports results to one decimal point.

10.3 Units of Measure

mg/dL

10.4 Clinically Reportable Range (CRR)

0.2 - 60.0 mg/dL

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 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…
<0.2 mg/dL	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: <0.2 mg/dL
≥12 mg/dL	**On Board Automated Dilution:** Results ≥12.0 mg/dL will automatically have repeat testing performed into the instrument using dilution factor of 1.5. No multiplication is necessary. ~~Append the result with code –REP.~~
>18.0 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 5 **Diluent**: Purified water. Enter dilution factor as a whole number on the "Enter Sample Data" screen. ~~Report the assay with code of –REP.~~
>60.0 mg/dL	If the recommended dilution does not give results within the clinically reportable range, report as: ">60.0 mg/dL-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.
~~Quantity not sufficient to repeat~~	~~Append –QNSR to the original result.~~

11. EXPECTED VALUES

11.1 Reference Ranges

Age	Female	Male

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Adult (>18 years):	< 0.9 mg/dL	< 0.9 mg/dL
Pediatric:		
0 – 90 days	0.1-1.6	0.1-1.6
3 – 12 months	0.1-0.8	0.1-1.1
13 months – 3 years	0.1-0.8	0.1-1.1
4 – 10 years	0.1-1.0	0.1-0.8
11 – 14 years	0.1-0.8	0.1-0.8
15 – 18 years	0.1-0.8	0.1-0.8

11.2 Critical Values

None established

11.3 Priority 3 Limit(s)

None established

12. CLINICAL SIGNIFICANCE

C-Reactive Protein is one member of a group of proteins known as "acute phase reactants". The circulating concentration of these proteins rises sharply and quickly following surgery, other tissue injury, or inflammation. CRP increases several hundredfold, with peak levels usually reached within 72 hours. A persistent elevation of CRP longer than one week after surgery may indicate the continuation of the pathologic process or a complication. High CRP is a nonspecific finding, i.e., it does not identify the specific disease process and/or its cause. It can be used to "screen" presumably "well" persons for the presence of disease.

Increased CRP levels may be present in bacterial infections, fungal infections, and some parasitic infestations; however, viral infections are less likely to cause substantial elevations. Other causes of an elevated CRP level may include: extensive physical trauma, myocardial infarction, pyelonephritis, and bacterial pneumonia. CRP levels may assist in distinguishing bacterial from aseptic meningitis in infants.

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 mg/dL	> 0.14 mg/dL
8.0 mg/dL	> 0.28 mg/dL

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

0.2 – 12.0 mg/dL

14.2 Precision

Material	Mean mg/dL	Standard Deviation (%CV)	
		Within-run	Between-day
Ciba Corning Immuno 2	0.7	0.03 (4.2)	0.05 (7.1)
Kallestad QM2/QM300	6.0	0.06 (1.0)	0.13 (2.1)

14.3 Interfering Substances

Lipemia (Intralipid®) of 1000 mg/dL will decrease CRP result of 2.3 mg/dL by 11%.

HIL Interference:
The CRP method was evaluated for interference from hemolysis, icterus and lipemia according to CLSI/NCCLS EP7-P. 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	CRP Conc mg/dL	Bias %
Hemoglobin (hemolysate)	1000 mg/dL (monomer)	1.6	<10
Bilirubin (unconjugated)	80 mg/dL	1.7	<10
Lipemia (Intralipid®)	600 mg/dL	2.3	<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 (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 CRP Flex® Reagent Cartridge DF37

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, CRP Flex® Reagent Cartridge DF37, Siemens Healthcare Diagnostics Inc., 03/9/2015.
3. Package insert, C-Reactive Protein Calibrator DC30, Siemens Healthcare Diagnostics Inc., 03/2015.
4. Package insert, Liquichek Immunology Controls, Bio-Rad Laboratories, 08/2010.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
			Supersedes SOP C107.001		
000	7/28/15	1, 7.1	Add analyzer name	L Barrett	R SanLuis
000	7/28/15	3.2	Specify anticoagulant	L Barrett	R SanLuis
000	7/28/15	4.2	Update hazard statement	L Barrett	R SanLuis
000	7/28/15	5.3	Edit calibration levels statement	L Barrett	R SanLuis
000	7/28/15	6.4,6.6	Replace LIS with Unity Real Time	L Barrett	R SanLuis
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000	7/28/15	15	Update to standard wording	L Barrett	R SanLuis
000	7/28/15	16	Update document titles	L Barrett	R SanLuis
000	7/28/15	Footer	Version # leading zero's dropped due to new EDCS in use as of 10/7/13	L Barrett	R SanLuis

19. ADDENDA

None