TRAINING UPDATE

Lab Location:	GEC	**Date Distributed:**	7/20/2021
Department:	Core Lab	**Due Date:**	8/20/2021

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:

Calcium by Dimension® EXL Chemistry Analyzer GEC.C269 v2

Description of change(s):

Note: *DI will flag the result with comment to repeat on other instrument.* This same DI rule applies across the lab system.

Section	Reason
10.6	Add repeat testing for below CRR

This revised SOP will be implemented on August 3, 2021

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

Technical SOP

Title	**Calcium by Dimension® EXL Chemistry Analyzer**
Prepared by	Demetra Collier Date: 9/8/2020
Owner	Robert SanLuis Date: 9/8/2020

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

TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Test Code
Calcium	Dimension® EXL Chemistry Analyzer	CA

Synonyms/Abbreviations
Ca

Department
Chemistry

2. ANALYTICAL PRINCIPLE

Calcium reacts with OCPC to form a purple complex. The amount of complex thus formed is proportional to the calcium concentration and is measured using a bichromatic (577, 540 nm) endpoint technique. Magnesium ions, which also form a colored complex with OCPC, are removed from the reaction by complexation with 8-quinolinol.

CA^{++} + OCPC ——pH 9.7——> Ca-OCPC complex (absorbs at 577 nm)

Mg^{++} + 8-quinolinol ——> Magnesium quinolinate (nonabsorbing at 577 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. Avoid prolonged contact of the serum and plasma with separated red cells.
Special Collection Procedures	None
Other	N/A

3.2 Specimen Type & Handling

Criteria		
Type	**-Preferred**	Plasma (Lithium Heparin)
	-Other Acceptable	Serum

Criteria		
Collection Container	Plasma: Mint green top tube (PST) Serum: Red top tube, Serum separator tube (SST)	
Volume - Optimum **- Minimum**	1.0 mL 0.5 mL	
Transport Container and Temperature	Collection container or plastic vial at room temperature	
Stability & Storage Requirements	Room Temperature:	8 hours, separate sample
	Refrigerated:	(2-8°C) 2 days
	Frozen:	(-20°C or colder) 45 days
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 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
Calcium	Siemens, Flex® reagent cartridge, Cat. No. DF23A

4.2 Reagent Preparation and Storage

Reagent	Calcium
Container	Reagent cartridge
Storage	Store at 2-8° C

Stability	• Stable until expiration date stamped on reagent cartridges. • Sealed wells on the instrument are stable for 30 days. • Open well stability - o One (1) day for wells 1-6 o 10 days for wells 7-8
Preparation	All reagents are liquid and ready to use.

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	• Remove vials from refrigerator and proceed directly to next step. • Remove stopper and add 2.00 ± 0.01 mL Purified Water Diluent or reagent grade water. The water should be at room temperature. • 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 2-8ºC for future use. Prior to use, invert 10 times and swirl gently.
Storage/Stability	• Store at 2 – 8°C. • The unopened calibrators are stable until the expiration date printed on the label • Assigned values are stable for 24 hours after reconstitution when stored at 2 – 8°C.

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	CHEM I Calibrator
Assay Range	5.0 – 15.0 mg/dL

Calibration levels	See reagent package insert for lot specific assigned values in mg/dL
Frequency	• Every new reagent cartridge lot. • Every 3 months 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 1.000 C_1 0.090
Procedure	Refer to Calibration / Verification Siemens Dimension® EXL procedure for specific instructions.

5.4 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 and 2	Bio-Rad Laboratories Cat. No. 691 and 692

6.2 Control Preparation and Storage

Control	Liquichek Unassayed Chemistry Controls, Level 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	**Thawed**: stable for 15 days at 2-8°C. **Frozen**: 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 EXL QC Schedule and the Dimension Quick Reference Guide.

6.4 Tolerance Limits and Criteria for Acceptable QC

Step	Action
1	Acceptable ranges for QC are programmed into the instrument's Quality Control software system and Unity Real Time, and may be posted near the instrument for use during computer downtime.
2	**Run Rejection Criteria** • Anytime the established parameters are exceeded (if one QC result exceeds 2SD), 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 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 EXL® 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

- Calibrated pipettes and disposable tips
- Reagent grade water (Millipore® or equivalent)
- Plastic serum tubes and serum cup

8. PROCEDURE

CA Flex® reagent cartridge Cat. No. DF23A is required to perform this test.

Calcium is performed on the Dimension EXL® 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 Maintenance, Siemens Dimension® EXL procedure.
2.	Check reagent inventory
3.	Sampling, reagent delivery, mixing, processing, and printing of results are automatically performed by the Dimension® EXL 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® EXL segments for analysis by the instrument. Refer to the Sample Processing, Dimension® EXL 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 EXL QC Schedule.
2.	Follow the instructions, outlined in the Dimension® EXL 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® EXL system manual "Error messages" section for troubleshooting.
4.	Follow protocol in Section 10.6 "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:	5 µL
Reagent 1 Volume:	145 µL
Reagent 2 Volume:	33 µL
Diluent Volume:	258 µL
Temperature:	37°C
Wavelength:	577 and 540 nm
Type of Measurement:	bichromatic rate

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

9. CALCULATIONS

The instrument automatically calculates and prints the concentration of calcium 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)

5.0 – 45.0 mg/dL

10.5 Review Patient Data

Technologist must review each result with error messages. Refer to the Dimension EXL® 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 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…
< 5.0 mg/dL	Result will be flagged in DI as *Repeat on a different Instrument.* Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Repeat on the other instrument. If same result obtained, verify sample is not contaminated with EDTA or diluted with IV fluid. Report as: < 5.0 mg/dL

IF the result is …	THEN…
> 15.0 mg/dL	**On Board Automated Dilution:** Results > 15.0 mg/dL will automatically have repeat testing performed into the instrument using dilution factor of 1.7. No multiplication is necessary.
> 25.5 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**: reagent grade water Enter dilution factor as a whole number on the "Enter Sample Data" screen.
> 45.0 mg/dL	If the recommended dilution does not give results within the clinically reportable range, report as: "> 45.0 mg/dL - REP" Check for integrity issues prior to releasing result.

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

11. EXPECTED VALUES

11.1 Reference Ranges

Age	Female	Male
Adult (>19 years):	8.4 – 10.6 mg/dL	8.4 – 10.6 mg/dL
Pediatric:		
16 –19 years	9.0 - 10.7	9.0 - 10.7
14 –15 years	9.3 - 10.7	9.3 - 10.7
12 –13 years	9.0 - 10.6	9.0 - 10.6
10 –11 years	9.0 - 10.1	9.0 - 10.1
7 – 9 years	9.0 - 10.1	9.0 - 10.1
4 – 6 years	9.0 - 10.1	9.0 - 10.1
1 – 3 years	8.9 - 9.9	8.9 - 9.9
6 – 11 months	8.1 - 11.0	8.0 - 10.9
91– 180 days	8.0 - 11.4	8.5 - 11.3
31– 90 days	8.2 - 11.0	8.7 - 11.2
8 – 30 days	8.6 - 11.8	8.8 - 11.6
0 – 7 days	7.8 - 11.2	7.6 - 11.3

11.2 Critical Values

All ages, male and female

Low < 6.0 mg/dL
High > 13.0 mg/dL

11.3 Standard Required Messages

None established

12. CLINICAL SIGNIFICANCE

Serum calcium is involved in the regulation of neuromuscular and enzyme activity, bone metabolism and blood coagulation. Calcium blood levels are controlled by a complex interaction of parathyroid hormone, vitamin D, calcitonin and adrenal cortical steroids. Calcium measurements are useful in the diagnosis of parathyroid disease, some bone disorders and chronic renal disease. A low level of calcium results in tetany.

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 EXL Operator's Guide.

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

Concentration	S.D.
7.0 mg/dL	>0.17 mg/dL
13.5 mg/dL	>0.23 mg/dL

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

5.0 – 15.0 mg/dL

14.2 Precision

Material	Mean mg/dL	Standard Deviation (%CV)	
		Within-run	Total
Moni-Trol® Control			
Level 1	9.2	0.08 (0.8)	0.16 (1.7)
Level 2	12.9	0.12 (0.9)	0.24 (1.9)
LYPHOCHEK® Urine Control			
Urine Normal	8.4	0.06 (0.7)	0.08 (0.9)

14.3 Interfering Substances

- Interference due to magnesium is negligible at magnesium levels normally encountered in human serum. A maximum positive interference of 0.7 mg/dL [0.17 mmol/L] occurs at a magnesium level of 7 mg/dL [2.9 mmol/L].
- Calcium values may be falsely decreased in the presence of gadolinium-containing contrast agents such as Omniscan™. The manufacturer recommends to avoid drawing samples for serum calcium 24 hours after administration of this.
- Bilirubin (unconjugated) of 80 mg/dL decreases calcium at 6.4 mg/dL by 11%.

HIL Interference:
The CA 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	CA Conc mg/dL	Bias %
Hemoglobin (hemolysate)	1000 mg/dL [0.62 mmol/L]	6.4	<10
Bilirubin	60 mg/dL [1026 µmol/L]	6.4	<10
Lipemia (Intralipid®)	200 mg/dL [2.26 mmol/L]	6.3	<10

14.4 Clinical Sensitivity/Specificity/Predictive Values

Not available

15. SAFETY

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

16. RELATED DOCUMENTS

1. Dimension EXL® Clinical Chemistry System Operator's Manual
2. Calibration / Verification Siemens Dimension® EXL procedure
3. Dimension EXL® Cal Accept Guidelines
4. Dimension EXL® Calibration summary
5. Sample Processing, Dimension® EXL procedure
6. Maintenance, Siemens Dimension® EXL procedure
7. Laboratory Quality Control Program
8. Dimension EXL QC Schedule
9. Laboratory Safety Manual
10. Safety Data Sheets (SDS)
11. Dimension EXL Limits Chart
12. Retention of Records and Materials (Lab Policy)
13. Dimension EXL® System Error Messages Chart
14. Centrifuge Use, Maintenance and Functions Checks (Lab policy)
15. Specimen Acceptability Requirements (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 CA Flex® Reagent Cartridge DF23A

17. REFERENCES

1. Ghoshal, Amit K. and Soldin, Steven J., Evaluation of the Siemens Dimension® RxL: Integrated chemistry system-pediatric reference ranges. Clinica Chimica Acta 2003; 331:144.
2. Package Insert, CA Flex® Reagent Cartridge DF23A, Siemens Healthcare Diagnostics Inc., 5/21/19
3. Package insert, CHEM I CAL DC18C, Siemens Healthcare Diagnostics Inc., 5/23/20
4. Package insert, Liquichek Unassayed Serum Chemistry Controls, Bio-Rad Laboratories, 3/2019

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
1	6/29/21	10.6	Add repeat testing for below CRR	L Barrett	R SanLuis

19. ADDENDA

None