

## TRAINING UPDATE

**Lab Location:** GEC  
**Department:** Core Lab

**Date Distributed:** 3/2/2021  
**Due Date:** 4/2/2021

### DESCRIPTION OF PROCEDURE REVISION

**Name of procedure:**

**High Sensitivity Troponin I by Dimension EXL® System  
GEC.C280 v2**

**Description of change(s):**

**Note: the same changes have been made to the Vista Tropi SOP**

Section	Reason
3.2	Specified rejection for hemolysis
8.2	Added note for values below 83 pg/mL

**This revised SOP will be implemented on March 16, 2021**

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

Technical SOP

<b>Title</b>	<b>High Sensitivity Troponin I by Dimension EXL® System</b>	
<b>Prepared by</b>	Demetra Collier	Date: 11/2/2020
<b>Owner</b>	Robert SanLuis	Date: 11/2/2020

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

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## 1. TEST INFORMATION

Assay	Method/Instrument	Test Code
High Sensitivity Troponin I	Dimension EXL® System	TROPI1

Synonyms/Abbreviations
Troponin, Tropi, TNIH

Department
Chemistry

## 2. ANALYTICAL PRINCIPLE

The Dimension EXL TNIH assay is a homogeneous, sandwich chemiluminescent immunoassay based on LOCI technology. The LOCI reagents include two synthetic bead reagents and two biotinylated anti-cardiac troponin I monoclonal antibody fragments. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with a third anti-cardiac troponin I monoclonal antibody and contains chemiluminescent dye. Sample is incubated with Chemibeads and biotinylated antibodies to form bead-cardiac troponin I-biotinylated antibody sandwiches. Sensibeads are added and bind to the biotin to form bead-pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads which diffuses into the Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is a direct function of the cardiac troponin I concentration in the sample.

## 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	
<b>Type</b> -Preferred -Other Acceptable	Plasma (Lithium Heparin) Serum
<b>Collection Container</b>	Plasma: Mint green top tube (PST) Serum: Red top tube, Serum separator tube (SST)
<b>Volume</b> - Optimum - Minimum	1.0 mL 0.5 mL
<b>Transport Container and Temperature</b>	Collection container or Plastic vial at room temperature
<b>Stability &amp; Storage Requirements</b>	Room Temperature: 8 hours
	Refrigerated: 24 hours
	Frozen: 40 days
<b>Timing Considerations</b>	Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of two hours from the time of collection.
<b>Unacceptable Specimens &amp; Actions to Take</b>	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.
<b>Compromising Physical Characteristics</b>	Gross hemolysis. Only reject sample if flagged for hemolysis by DI. Credit the test with the appropriate LIS English text code explanation of HMT (Specimen markedly hemolyzed) and request a recollection
<b>Other Considerations</b>	Allow Red Top or SST to clot completely prior to centrifugation.

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

## 4. REAGENTS

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

### 4.1 Reagent Summary

Reagents	Supplier & Catalog Number
High Sensitivity Troponin I	Siemens, Flex® reagent cartridge, Cat. No. RF627
CTNI Sample Diluent	Siemens Healthcare Diagnostics Cat. No. KD692

#### 4.2 Reagent Preparation and Storage

<b>Reagent</b>	<b>High Sensitivity Troponin I</b>
<b>Container</b>	Reagent cartridge
<b>Storage</b>	Store at 2-8°C
<b>Stability</b>	<ul style="list-style-type: none"> <li>• Stable until expiration date stamped on reagent cartridges.</li> <li>• Sealed wells on the instrument are stable for 30 days.</li> <li>• Open wells: 7 days for wells 1 - 8</li> </ul>
<b>Preparation</b>	All reagents are liquid and ready to use.

<b>Reagent</b>	<b>CTNI Sample Diluent</b>
<b>Container</b>	Reagent bottle
<b>Storage</b>	Store at 2-8°C
<b>Stability</b>	<ul style="list-style-type: none"> <li>• <b>Unopened:</b> stable until expiration date stamped on bottle</li> <li>• <b>Opened:</b> 30 days when recapped and stored at 2-8°C.</li> </ul>
<b>Preparation</b>	CTNI SDIL is ready for use. No preparation is required.

### 5. CALIBRATORS/STANDARDS

#### 5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
LOCI TNIH CAL	Siemens Dimension EXL®, Cat. No. RC627

#### 5.2 Calibrator Preparation and Storage

<b>Calibrator</b>	High Sensitivity Troponin I Calibrator ( LOCI TNIH CAL)
<b>Preparation</b>	Before use, thaw at room temperature (18–30°C) for one hour (no more than two hours), swirl and invert gently to mix.
<b>Storage/Stability</b>	<ul style="list-style-type: none"> <li>• Store at -15°C to -25°C</li> <li>• <b>Unopened Frozen:</b> stable until expiration date on the box.</li> <li>• <b>Unopened Thawed:</b> 3 days when stored at 2-8°C</li> <li>• <b>Opened Calibrator:</b> stable for 3 days when thawed, recapped and stored at 2-8°C.</li> </ul>

#### 5.3 Calibration Parameter

Criteria	Special Notations
<b>Reference Material</b>	LOCI TNIH CAL
<b>Assay Range</b>	4 – 25000 pg/mL
<b>Suggested Calibration Level</b>	See Reagent Package Insert for lot specific assigned values in pg/mL

<b>Frequency</b>	<ul style="list-style-type: none"> <li>• Every new reagent cartridge lot.</li> <li>• Every 21 days for any one lot</li> <li>• When major maintenance is performed on the analyzer.</li> <li>• When control data indicates a significant shift in assay.</li> </ul>
<b>Calibration Scheme</b>	5 levels, n = 5
<b>Procedure</b>	Refer to Calibration / Verification Siemens Dimension® EXL procedure for specific instructions.

#### 5.4 Tolerance Limits

<b>IF.....</b>	<b>THEN.....</b>
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

<b>Controls</b>	<b>Supplier and Catalog Number</b>
Liquichek™ Cardiac Markers Plus Control LT Levels 1B, 2 and 3	Bio-Rad Laboratories Cat # 27105, 147 and 148

#### 6.2 Control Preparation and Storage

<b>Control</b>	Liquichek Cardiac Markers Plus Control LT, Level 1B, 2 and 3
<b>Preparation</b>	Allow the frozen control to thaw at room temperature (18-25°C) for approximately 30 minutes or until completely thawed. Swirl the contents gently to ensure homogeneity. (Do not use a mechanical mixer). Immediately load the vial on the analyzer. After each use, promptly replace the stopper and return to 2-8°C storage.
<b>Storage/Stability</b>	<b>Frozen:</b> stable until the expiration date at -20 to -70° C. <b>Thawed and Opened:</b> Once the stopper is punctured, stable for 5 days when stored at 2-8°C. Once thawed, do not re-freeze

#### 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 EXL® 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	<b>Run Rejection Criteria</b> <ul style="list-style-type: none"><li>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.</li><li>The technologist must follow the procedure in the Laboratory QC Program to resolve the problem.</li></ul>
3	<b>Corrective Action:</b> <ul style="list-style-type: none"><li>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.</li><li>Corrective action documentation must follow the Laboratory Quality Control Program.</li></ul>
4	<b>Review of QC</b> <ul style="list-style-type: none"><li>QC must be reviewed weekly by the Group Lead or designee and monthly by the Supervisor/Manager or designee.</li><li>If the SD and/or CV are greater than established ranges, investigate the cause for the imprecision and document implementation of corrective actions.</li></ul>

#### 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 -15 to -25°C for calibrator
- Freezer capable of sustaining range not to exceed -20 to -70°C for QC product
- Centrifuge

### 7.3 Supplies

- HM Reaction Vessels (Cat No. RXV1A)
- System Fluids
- Assorted calibrated pipettes (MLA or equivalent) and disposable tips

## 8. PROCEDURE

TNIH Flex® reagent cartridge Cat. No. RF627 is required to perform this test.

High Sensitivity Troponin I 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.**



<b>8.1</b>	<b>Instrument Set-Up Protocol</b>
1.	For instrument set up and operation: Refer to Startup and 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.”

<b>8.2</b>	<b>Specimen/Reagent Preparation</b>
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.

<b>8.3</b>	<b>Specimen Testing</b>
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. <b>Note:</b> DI will not flag Delta failures if the result is < 83pg/mL; DI will add the comment code RVT to the result.
5.	Append the appropriate English text code qualifier messages to any samples requiring a comment regarding sample quality and/or any other pertinent factors.

<b>Test Conditions</b>	
Sample Volume:	10 µL
Chemibead Reagent Volume:	20 µL
Biotinylated Antibody Volume:	20 µL
Sensibead Reagent Volume:	20 µL
Assay Buffer Volume:	100 µL
Reaction Time:	10 minutes
Test Temperature:	37° C
Wavelength:	680 and 612 nm
Type of measurement:	Chemiluminescence

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

**9. CALCULATIONS**

The instrument automatically calculates the concentration of High Sensitivity Troponin I in pg/mL.

**10. REPORTING RESULTS AND REPEAT CRITERIA**

**10.1 Interpretation of Data**

None required

**10.2 Rounding**

No rounding is necessary. Instrument reports result as whole number.

**10.3 Units of Measure**

pg/mL

**10.4 Clinically Reportable Range (CRR)**

4 – 125,000 pg/mL

**10.5 Review Patient Data**

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

**10.6 Repeat Criteria and Resulting**

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

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

<b>IF the result is ...</b>	<b>THEN...</b>
< 4 pg/mL	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: < 4 pg/mL
≥ 25,000 pg/mL	Manually dilute the specimen using CTNI Sample Diluent to obtain results within the reportable range. The maximum dilution factor is x5. Enter this dilution factor when manually programming the sample dilution.

IF the result is ...	THEN...
> 125,000 pg/mL	If the recommended dilution does not give results within the clinically reportable range, report as: “> 125,000 pg/mL-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

< 83 pg/mL

### 11.2 Critical Values

Initial (first) critical value: > 100 pg/mL

Treatment of **subsequent critical values** is based on delta criteria:

Prior Critical Value	Delta Threshold	Example
101 - 500 pg/mL	Value doubles	Prior value of 101, next value must be 202 or greater
501 – 1,000 pg/mL	Increase of 250	Prior value of 600, next value must be 850 or greater
1,001 pg/mL or more	Increase of 1,000	Prior value of 2,000, next value must be 3,000 or greater

**If the subsequent critical value does NOT qualify to be called**, document this by appending the code **TROPC** to the result. This code translates to “Laboratory value indicates a critical value previously reported.”

#### Notes:

- Data Innovations (DI) will flag results that meet delta criteria to be called (Error code contains ‘CALL’ and the Error name contains ‘CALL TROP’).
- When DI is down, ALL critical troponin values must be called.

### 11.3 Standard Required Messages

None established

## 12. CLINICAL SIGNIFICANCE

Troponin 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.

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.

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.

### 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.

The expected maximum observed standard deviations for repeatability using n = 5 replicates at the following Cardiac Troponin I concentrations are:

<b>TNIH Concentration</b>	<b>Acceptable S.D. Maximum</b>
50.0 pg/mL	4.8 pg/mL
500.0 pg/mL	33.5 pg/mL

### 14. **LIMITATIONS OF METHOD**

#### 14.1 **Analytical Measurement Range (AMR)**

4 – 25,000 pg/mL

## 14.2 Precision

Material	Mean pg/mL	Standard Deviation (%CV)	
		Repeatability	Within-Lab
Plasma 1	48.0	2.3	6.0
Plasma 2	71.8	2.0	3.3
Plasma 3	155.7	1.8	3.0

## 14.3 Interfering Substances

- Patient samples may contain cardiac troponin-specific autoantibodies that could react in immunoassays to give depressed results.
- Specimens that contain biotin at a concentration of 300 ng/mL demonstrate a less than 10% change in results. Biotin concentrations greater than this may lead to falsely depressed results for patient samples. Testing specimens from renal dysfunction patients taking biotin may lead to false negative results. Therefore, do not use this device in patients with renal impairment (eGFR<60), unless it is confirmed that the patient is not taking biotin. Patients taking more than 20 mg/day of biotin may have falsely negative results, and should not use this test.
- Dextran 40 at 60 g/L increases the troponin result in plasma at 35.1 pg/mL and 1337.4 pg/mL by 22% and 4% respectively.
- Protein Gamma Globulin at 6 g/dL increases the troponin result in plasma samples at approximately 40 pg/mL and 1000 pg/mL of troponin.

### HIL Interference:

The TNIH assay was evaluated for interference according to CLSI EP07-A2.36 Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Lithium heparin plasma test sample ranges were: 40 ± 20 pg/mL and 1350 ± 650 pg/mL. Bias exceeding 10% is considered interference.

Substance tested	Substance Concentration	Bias %
Hemoglobin (hemolysate)	400 mg/dL	<10
Bilirubin (unconjugated)	40 mg/dL	<10
Bilirubin (conjugated)	30 mg/dL	<10
Lipemia Intralipid	3000 mg/dL	<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.

TNIH Flex® Reagent Cartridge may cause an allergic skin reaction.  
Contains: 5-chloro-2-methyl-3(2h)-isothiazolone mixture with 2-methyl-3(2h)-isothiazolone.  
Wear protective gloves/protective clothing/eye protection/face protection.  
IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention.

TNIH CAL may cause an allergic skin reaction.  
Contains: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1).  
Wear protective gloves/protective clothing/eye protection/face protection.  
IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention.

## 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. QC Schedule for Siemens Dimension EXL®
9. Laboratory Safety Manual
10. Safety Data Sheets (SDS)
11. Dimension EXL Limits Chart
12. Quest Diagnostics Records Management Procedure
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](http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls)
19. Current package insert TNIH Flex® Reagent Cartridge RF627

## 17. REFERENCES

1. Package Insert, TNIH Flex® Reagent Cartridge RF627, Siemens Healthcare Diagnostics Inc., 6/11/2019.
2. Package Insert, LOCI TNIH CAL, Siemens Healthcare Diagnostics Inc., 06/2020.
3. Package Insert, Liquichek Cardiac Markers Plus Control LT, Levels 1, 2, 3, 1A, 1B and 1C; Bio-Rad Laboratories, 06/2020.
4. Package Insert, CTNI Sample Diluent, Siemens Healthcare Diagnostics Inc., 04/2019.

**18. REVISION HISTORY**

<b>Version</b>	<b>Date</b>	<b>Section</b>	<b>Reason</b>	<b>Reviser</b>	<b>Approval</b>
1	2/25/21	3.2	Specified rejection for hemolysis	L Barrett	R SanLuis
1	2/25/21	8.2	Added note for values below 83 pg/mL	L Barrett	R SanLuis

**19. ADDENDA**

None