DXI 600 100 hs Troponin

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Approval and Periodic Review Signatures

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1.0	Approved and Current	Initial version	2/5/2024	2/7/2024	Indefinite

PRINCIPLE

Access hsTnI is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of Cardiac Troponin I (cTnI) levels in human serum and plasma using the UniCel DxI Access Immunoassay Systems to aid in the diagnosis of Myocardial Infarction (MI).

The Troponins (I, C, and T) are members of a complex of proteins that modulate the calcium-mediated interaction between actin and myosin within muscle cells.[1] The nomenclature of these distinct proteins of the Troponin complex is derived from their respective function in muscle contraction. Troponin T anchors the Troponin complex to Tropomyosin of the thin filament, whereas Troponin I inhibits Actomyosin ATPase, and Troponin C is a calcium-binding subunit. Three isoforms of Troponin I (TnI) have been identified: one associated with fast-twitch skeletal muscle, one with slow-twitch skeletal muscle, and one with cardiac muscle. The slow and fast-twitch isoforms have a similar molecular weight of approximately 20,000 dalton (Da) each. The cardiac-specific TnI isoform has a molecular weight of approximately 24,000 Da and contains a post-translational tail of 31 amino acids on the N- terminus of the molecule.[2,3] This sequence and the 42% and 45% dissimilarity with the sequences of the other two isoforms have made possible the generation of highly specific monoclonal antibodies without cross-reactivity with other non-cardiac TnI forms.[4,5]

As a result of its high tissue specificity cTnI is a cardio-specific, highly sensitive marker for myocardial injury. The Access hsTnI assay uses monoclonal antibodies specifically directed against human cTnI.

In myocardial infarction, cTnI levels rise in the hours after the onset of cardiac symptoms, reaching a peak at 12-16 hours, and can remain elevated for 4-9 days post MI.[6,7] Numerous

pathologies can potentially cause Troponin elevations without overt ischemic heart disease.[8,9] These pathologies include, but are not limited to, congestive heart failure, acute and chronic trauma, electrical cardioversion, hypertension, hypotension, arrhythmias, pulmonary embolism, severe asthma, sepsis, critical illness, myocarditis, stroke, non-cardiac surgery, extreme exercise, drug toxicity (for e.g. Adriamycin, 5-fluorouracil, Herceptin and snake venoms), end stage renal disease, and rhabdomyolysis with cardiac injury.[9,10] Importantly, these other etiologies rarely demonstrate the classic rising and falling pattern experienced with a MI, which highlights the importance of serial monitoring when the clinical scenario is unclear.[8,11]

Cardiac Troponin should be measured upon admission, and then serially thereafter at regular intervals in order to demonstrate a rise and/or fall in cTn values. When an increased cTn value does not support the diagnosis of acute myocardial ischemia, a careful search for other possible etiologies of myocardial injury should be undertaken.[12]

METHODOLOGY

The Access hsTnI assay is a two-site immunoenzymatic ("sandwich") assay. Monoclonal anti-cTnI antibody conjugated to alkaline phosphatase is added to a reaction vessel along with a surfactant-containing buffer and sample. After a short incubation, paramagnetic particles coated with monoclonal anti-cTnI antibody are added. The human cTnI binds to the anti-cTnI antibody on the solid phase, while the anti-cTnI antibody-alkaline phosphatase conjugate reacts with different antigenic sites on the cTnI molecules. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production

is directly proportional to the concentration of cTnI in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

SPECIMEN

SPECIMEN COLLECTION AND PREPARATION

1. Serum and lithium heparin plasma are the recommended sample types.

2. The role of pre-analytical factors in laboratory testing has been described in a variety of published literature.[17,18] To minimize the effect of pre-analytical factors observe the following recommendations for handling, processing, and storing blood samples:

    - Centrifuge samples for 1 min at 1000 rpm.[17]
    - Collect all blood samples observing routine precautions for venipuncture.
    - Allow serum samples to clot completely before centrifugation in a vertical, closure-up position.
    - Keep tubes stoppered at all times.
    - Store samples, tightly stoppered at room temperature (15 °C to 25 °C) for up to 4 hours.
    - If the assay will not be completed within 4 hours, refrigerate the samples at 2 °C to 8 °C.
    - If the assay will not be completed within 48 hours, freeze the serum at -20 °C or colder.

- Frozen specimens can be stored for up to 180 days before testing.
- **Thaw samples only once.** Prior to analysis, frozen samples should first be thawed at room temperature, mixed thoroughly by gentle inversion, and then centrifuged, as per tube manufacturer's recommendations.

3. The following guidelines should be followed when preparing specimens:

   - Ensure that any residual fibrin and cellular matter has been removed ***prior to*** analysis. Failure to do so can contribute to falsely elevated results.[19]
   - For plasma, avoid transferring material from the white blood cell/platelet layer, located just above the red blood cells. If a fixed angle rotor is used for centrifugation, ***be careful not to re-suspend platelets***.
   - Transfer turbid serum or plasma samples from their original tube and centrifuge again ***prior to*** assay. Never centrifuge a specimen in an original tube that contains a separating device (gel barrier) more than once.
   - Follow blood collection tube manufacturer's recommendations for centrifugation.

4. Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, at times, from lot to lot.

REAGENTS

PRODUCT INFORMATION

1. **Access hsTnI Reagent Pack**

2. **Cat. No. 852699: 100 determinations, 2 packs, 50 tests/pack:**

   - Provided ready to use.
   - Store upright and refrigerate at 2 °C - 10 °C.
   - Stable until the expiration date stated on the label when stored at 2 °C - 10 °C.
   - Stable at 2 °C - 10°C for 64 days after initial use.
   - Signs of possible deterioration are a broken elastomeric layer on the pack or quality control values out of range.
   - If the reagent pack is damaged (e.g., broken elastomer), discard the pack.

Well	Ingredients
Rla:	Dynabeads* paramagnetic particles coated with mouse monoclonal anti-human cTnI antibody suspended in TRIS buffered saline, with surfactant, bovine serum albumin (BSA),< 0.1% sodium azide and 0.1% ProClin** 300.
Rlb:	0.lN NaOH
Rlc:	TRIS buffered saline, surfactant, protein (mouse),< 0.1% sodium azide and 0.1% ProClin 300.
Rid:	Sheep monoclonal anti-human cTnI alkaline phosphatase conjugate diluted in ACES buffered saline, with surfactant, BSA matrix, protein (bovine, sheep, mouse), < 0.1% sodium azide and 0.25% ProClin 300.

*Dynabeads is a registered trademark of Dynal A.S., Oslo, Norway.

**ProClin™ is a trademark of The Dow Chemical Company ("Dow") or an affiliated company of Dow.

WARNINGS AND PRECAUTIONS

- **For *in vitro* diagnostic use only.**
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, regardless of their origin, treatment, or prior certification, these products should be handled as potentially infectious according to universal precautions and good clinical laboratory practices. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.

SDS	Safety Data Sheet is available at techdocs.beckmancoulter.com

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

1. Access hsTnI Calibrators:-
   - Provided at 0 and at approximately 30.7, 144, 567, 2,293, 9,280 and 27,027 pg/mL (ng/L).
   - Cat. No. C26909.
2. Quality Control (QC) materials: commercial control material.
3. Access Sample Diluent A
   - Vial Cat. No. 81908
   - Diluent Pack Cat. No. A79783 (For use with the UniCel DxI system onboard dilution feature.)
4. Access Substrate
   - Cat. No. 81906
5. UniCel DxI Access Immunoassay Systems:

- UniCel DxI Wash Buffer II, Cat. No. A16793

EQUIPMENT AND MATERIALS

- Beckman Coulter Unicel DxI 600 Analyzer
- Rl Access hsTnI Reagent Packs

CALIBRATION

An active calibration curve is required for all tests. For the Access hsTnI assay, calibration is required every 63 days. Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

QUALITY CONTROL

During operation of the Beckman Coulter UniCel DxI 600 analyzer, at least two levels of Bio-Rad Cardiac Troponin quality control materials should be tested at the beginning of each shift (or at minimum every 8 hours). In addition, controls should be performed after calibration with each new lot of reagent, and after specific maintenance or troubleshooting steps described in the appropriate Beckman Coulter AU analyzer User Guide/Instructions for Use (IFU)

TESTING PROCEDURE(S)

PROCEDURAL COMMENTS

1. Refer to the appropriate system manuals and/or Help system for a specific description of installation, start-up, principles of operation, system performance characteristics, operating instructions, calibration procedures, operational limitations and precautions, hazards, maintenance, and troubleshooting.

2. Mix contents of new (unpunctured) reagent packs by gently inverting pack several times before loading onto the instrument. Do not invert open (punctured) packs.

3. Use fifty-five (55) µL of sample for each determination, in addition to the sample container and system dead volumes, when requesting the Access hsTnI assay. Use fifty (50) µL of sample in addition to the sample container and system dead volumes for each determination run with the UniCel DxI Access Immunoassay system onboard dilution feature (test name: dTIhs). Refer to the appropriate system manuals and/or Help system for the minimum sample volume required.

PROCEDURE

Refer to the appropriate system manuals and/or Help system for information regarding managing samples, configuring tests, requesting tests, and reviewing test results.

- Select TnIhs as the test name for assaying samples containing cTnI concentrations up to the concentration of the Access hsTnI S6 calibrator.

- UniCel DxI Access Immunoassay System users may use the onboard dilution feature (Test name: dTIhs) for assaying samples containing cTnI concentrations greater than the Access hsTnI S6 calibrator.

RESULTS INTERPRETATION

Test results are automatically determined by the system software. The amount of analyte in the sample is determined from the measured light production by means of the stored calibration data. Test results can be reviewed using the appropriate screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing sample results.

REPORTING RESULTS

Refer to Appendix A for Reference Range.

PROCEDURAL NOTES

LIMITATIONS

1. Ambient laboratory temperature should be maintained between l8 °C and 30 °C (66.4 °F and 86.0 °F) while conducting patient sample testing. This assay employs an algorithm to correct for laboratory temperature fluctuations that could impact the accuracy of Troponin test results. Up to 8% residual systematic bias may be observed when comparing patient results obtained at l8 °C and 30 °C (64.4 °F and 86.0 °F).
2. The performance of Access hsTnI represented in these Instructions for Use is reflective of use on UniCel DxI Access Immunoassay Systems only. Performance on Access 2 Immunoassay Systems is not interchangeable. When using results from different systems, comparability of patient results should be verified within the laboratory, following guidelines such as those described in CLSI EP31-A-IR.[21]
3. Samples can be accurately measured within the analytical range of the Limit of Quantitation (LoQ), and the highest (S6) calibrator value [approximately 2.3 to 27,027 pg/mL (ng/L)].
    - If a sample contains less than the LoQ for the assay, the result will be reported as less than that value [i.e. < 2.3 pg/mL (ng/L)].

- If a sample contains more than the stated value of the highest Access hsTnI Calibrator (S6), the result will be reported as greater than that value. Alternatively, testing personnel may dilute one volume of sample with 9 volumes of Access Sample Diluent A.
- Refer to the appropriate system manuals and/or Help system for instructions on how to request a sample dilution on the instrument. The system will report the results adjusted for the dilution.

4. Onboard Dilution Feature for use on UniCel DxI Access Immunoassay systems:

- The UniCel DxI Access Immunoassay System onboard dilution feature automates the dilution process, using one volume of sample with 9 volumes of Access Sample Diluent A, allowing samples to be quantitated up to l0X the stated value of the highest calibrator (S6). The system reports the results adjusted for the dilution.

5. Samples with very high cTnI concentrations may cause carryover into the Access hsTnI reagent pack. The extent of carryover observed is directly proportional to the cTnI concentration that is present in the high sample. If a sample with cTnI >270,000 pg/mL (ng/L) is tested, clinically significant carryover may be observed with all subsequent samples that are tested from the same reagent pack. In one study, the estimated carryover (based upon the upper and lower limits of the 95% Cl) was 3-5 pg/mL (ng/L) from a high sample at 270,000 pg/mL (ng/L) and 5-8 pg/mL (ng/L) from a high sample at 500,000 pg/mL (ng/L). If there is suspected carryover into the reagent pack, use a fresh reagent pack and repeat all samples that were tested after the high cTnI sample.
6. For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have: (1) been regularly exposed to animals, (2) received immunotherapy or (3) had diagnostic procedures utilizing immunoglobulins

or immunoglobulin fragments, may produce human anti-animal antibodies, e.g. HAMA, that may interfere with immunoassays. Additionally, other antibodies such as human anti-goat antibodies may be present in patient samples.[22, 23] Such interfering antibodies may cause erroneous results. Carefully evaluate the results of those patients suspected of having these antibodies.

7. Other potential interferences in the patient sample could be present and may cause erroneous results in immunoassays. Some examples that have been documented in literature include rheumatoid factor and fibrin.[24] Carefully evaluate results if the sample is suspected of having these types of interferences.

8. Endogenous alkaline phosphatase (ALP), exogenous ALP and proteins capable of binding to ALP may cause interference.[25] Elevated ALP levels are commonly observed in patients with hepatobiliary disease and bone disease associated with increased osteoblastic activity. **Alkaline phosphatase levels above 400 U/L may cause false positive results**. In one study, a sample with cTnI concentration of approximately 8 pg/mL demonstrated an increase of 4 pg/mL when spiked with 800 U/L of alkaline phosphatase.

9. ***Access hsTnI should not be used for patients taking asfotase alfa (i.e. Strensiq).***[26]

10. Native human cardiac Troponin I was used in the development of this assay. Troponin I not from this source (e.g. recombinant antigens) may behave differently.

11. The Access hsTnI results should be interpreted in light of the total clinical presentation of the patient, including: symptoms, clinical history, data from additional tests, and other appropriate information.

12. Positive predictive values (PPV) demonstrated for female subjects using the established female 99th percentile URL values were lower than the PPV values obtained using the overall 99th percentile URL values. Using the lower female 99th percentile URLs may result in a higher proportion of positive test results for females that are non-MI. ***Taking into consideration the lower bound of the 95% Cl, in the worst-case scenario (serum drawn at 6-9 hours after admission) up to 75% of positive test results for females may be non-MI.***
13. Troponin results differ between methods due to selection of standardization or traceability.[27, 28] Do not use results between Troponin methods interchangeably.
14. The Access hsTnI assay does not demonstrate a "hook" effect up to 2,000,000 pg/mL (ng/L).

PERFORMANCE CHARACTERISTICS

LINEARITY

The Access hsTnI assay demonstrated acceptable linearity throughout the analytical measuring range. Linearity was tested using a protocol based on CLSI EP6-A.[33] Serum and lithium heparin plasma samples were evaluated. In each study, one high sample, approximately at the highest calibrator, and one low sample, approximately at the limit of detection, were mixed in order to make 7 sample concentrations evenly distributed across the analytical measuring range. Four replicates of the 7 mixed samples, 8 replicates of the low sample, and 4 replicates of the high sample were tested on a single UniCel/DxI 800 Access Immunoassay System.

The Access hsTnI assay was designed to be linear, with a maximum percent bias of 10% for samples

across the analytical measuring range. One study, analyzed using a linear regression method, demonstrated a maximum deviation from linearity of 10% for samples across the analytical measuring range.

IMPRECISION

Imprecision was tested using a protocol based on CLSI EP05-A3.[34] Studies were performed using a total of 3 reagent lots, 1 calibrator lot and multiple UniCel DxI 800 Access Immunoassay Systems. Serum and lithium heparin plasma samples were evaluated.

Representative data is shown in Table 5.0. Five patient pools were assayed in duplicate, on 3 reagent lots, in 4 runs per day, over 10 days generating a total of 40 runs and 240 replicates for each sample.

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DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE

STANDARD OPERATING POLICY AND PROCEDURE MANUAL

DXI 600/124 **High sensitivity Troponin I**

Table 5: Imprecision Study Results

Sample	Mean pg/mL (ng/L) (n=240)	Within-Run		Between-Run		Between-Day		Within-Lab		Total Imprecision*	
		%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)
Lithium Heparin Plasma											
Pool 1 Native	9.73	4	0.35	2	0.20	1	0.11	4	0.42	6	0.58
Pool 2 Native	19.37	3	0.62	1	0.26	0.2	0.04	4	0.67	6	1.1
Pool 3 Spiked	89	3	2.9	3	2.7	0.2	0.15	4	3.9	9	7.6

Table 5 (Cont'd): Imprecision Study Results

Sample	Mean pg/mL (ng/L) (n=240)	Within-Run		Between-Run		Between-Day		Within-Lab		Total Imprecision*	
		%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)
Pool 4 Spiked	4,990	3	170	4	182	0	0.84	5	249	10	480
Pool 5 Spiked	17,208	4	603	2	323	2	257	4	731	6	1,032
Serum											
Pool 1 Native	10.39	5	0.49	2	0.23	1	0.11	5	0.56	7	0.72
Pool 2 Native	12.24	5	0.55	3	0.38	1	0.10	6	0.68	6	0.78
Pool 3 Spiked	109	4	4.1	2	1.8	1	1.3	4	4.2	9	9.4

Table 5 (Cont'd): Imprecision Study Results

Serum											
Pool 4 Spiked	4,450	4	177	1	53	2	76	5	200	9	389
Pool 5 Spiked	18,254	4	788	1	168	1	120	5	814	7	1,300

*Total imprecision estimate includes within-run, between-run, between-day, between-lot and between-instruments and between-calibration variance components.

A reproducibility study was also conducted at all three independent testing facilities used in the clinical trial, in order to determine reproducibility across sites. The study was based on CLSI EP05-A3[34] guidelines and used four patient pools covering the measuring range of the assay, including one pool with concentration targeted near the 99th percentile URL, and four commercial controls. Samples were assayed in duplicate with 2 runs per day for 5 days at the 3 sites, generating a total of 30 runs and 60 replicates.

Table 6: Reproducibility Study Results

Sample	Mean pg/mL (ng/L)	N	Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
			%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)
Lithium Heparin Plasma												
Pool 1 Native	12.3	60	3	0.32	2	0.23	1	0.15	1	0.11	4	0.44
Pool 2 Spiked	31	60	3	0.96	2	0.73	0	0.0	2	0.57	4	1.3
Pool 3 Spiked	106	60	3	2.9	1	1.1	1	0.76	3	2.9	4	4.3
Pool 4 Spiked	19,792	60	3	626	2	401	0	0.00	2	309	4	805
Serum												
Pool 1 Native	11.6	60	4	0.43	2	0.21	0	0.00	2	0.17	4	0.5
Pool 2 Spiked	30	60	3	0.79	2	0.72	1	0.28	3	0.88	5	1.4
Pool 3 Spiked	111	60	3	3.3	1	1.4	0.3	0.38	4	4.6	5	5.8
Pool 4 Spiked	17,681	60	3	468	3	460	2	399	2	339	5	840

Table 6 (Cont'd): Reproducibility Study Results

Sample	Mean pg/mL (ng/L)	N	Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
			%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)	%CV	SD pg/mL (ng/L)
QC Material												
QC 1	24.7	60	4	0.99	3	0.73	3	0.66	4	1.0	7	1.7
QC 2	63	59	2	1.3	3	1.8	4	2.6	3	1.7	6	3.8
QC 3	1,273	60	2	27	2	22	3	39	3	33	5	62
QC 4	15,362	60	3	502	2	339	2	297	0	0.00	4	675

ANALYTICAL SPECIFICITY/INTERFERENCES

Lithium heparin plasma and serum samples containing cTnI concentrations of approximately 10 pg/mL (ng/L) and 100 pg/mL (ng/L) were spiked with the substances below and run on a single UniCel DxI 800 Access Immunoassay System. Values were calculated as described in CLSI EP7-A2.[35]

Interference was determined by testing controls (no interfering substance added) and matched test samples (with interfering substance added). There was no significant interference observed at the levels tested in Table 7.0. The change in concentration between the controls and test samples was within ±10% for samples > 11.5 pg/mL (ng/L). For samples, 11.5 pg/mL (ng/L) the change in concentration between controls and test samples was within 2SD, where 2SD is defined as 2.30 pg/mL (ng/L).

Table 7: Interfering Substances Tested

Substance	Concentration Added	Substance	Concentration Added
Acetaminophen	50 mg/dL	Fibrinogen	1,000 mg/dL
Acetylsalicylic Acid	65 mg/dL	Furosemide	40 mg/dL
Atenolol	1 mg/dL	Hemoglobin	4 mg/mL
Atorvastatin	20 µg/mL	Human Serum Albumin	6,000 mg/dL
Bilirubin (conjugated)	40 mg/dL	Ibuprofen	50 mg/dL
Bilirubin (unconjugated)	20 mg/dL	lntralipid	3,000 mg/dL
Bivalirudin	42 µg/mL	Sodium Heparin	28.8 U/mL
Caffeine	10 mg/dL	Methyldopa	2.5 mg/dL
Captopril	5 mg/dL	Nitrofurantoin	6.4 mg/dL
Cinnarizine	40 mg/dL	Nystatin	2 mg/dL
Clopidogrel	75 µg/mL	Phenobarbital	20 µg/mL
Cocaine	2 mg/dL	Rifampicin	60 µg/mL
Cyclosporine	5 µg/mL	Rosuvastatin	20 µg/mL
Digoxin	200 ng/mL	Tissue Plasminogen Activator (TPA)	2.5 µg/mL
Dopamine	65 mg/dL	Verapamil	16 mg/dL

A study was performed to evaluate the potential cross-reactivity of the assay with other substances that are similar in structure to cTnI. Lithium heparin plasma and serum samples containing cTnI concentrations of approximately 10 pg/mL (ng/L) and 100 pg/mL (ng/L) were spiked with the substances below and run on a single UniCel DxI 800 Access Immunoassay System. Values were calculated as described in CLSI EP7-A2.[35] There was no significant cross reactivity observed at the levels tested in Table 8.0. The change in concentration between the controls and test samples was within ±10% for samples > 11.5 pg/mL (ng/L). For samples ≤ 11.5 pg/mL (ng/L) the change in concentration between controls and test samples was within 2SD, where 2SD is defined as 2.30 pg/mL (ng/L).

Table 8: Cross-Reactants Tested

Substance	Concentration Added (ng/mL)
Actin	1,000
CK-MB	1,000
Myoglobin	1,000
Myosin	1,000
Cardiac Troponin C	250
Skeletal Troponin I	250
Tropomyosin	1,000
Cardiac Troponin T	125

LIMIT OF BLANK

Limit of Blank (LoB) was tested using a protocol based on CLSI EP17-A2.[36] Studies were performed using a total of 3 reagent lots, 3 calibrator lots and multiple UniCel DxI 600 and 800 Access Immunoassay Systems. In each study, 5 replicates of four zero analyte samples (S0

Calibrator & Sample Diluent A) were measured in 3 runs. The LoB for the Access hsTnI assay ranged from 0.0 to 1.7 pg/mL (ng/L) across the studies performed. The maximum observed LoB for Access hsTnI is 1.7 pg/mL (ng/L).

LIMIT OF DETECTION

Limit of Detection (LoD) was tested using a protocol based on CLSI EP17-A2.[36] Studies were performed using a total of 3 reagent lots, 3 calibrator lots and multiple UniCel DxI 600 and 800 Access Immunoassay Systems. Serum and lithium heparin plasma samples were evaluated. In each study, 5 replicates from five low-level samples were measured in 10 runs. The LoD for the Access hsTnI assay ranged from 1.5 to 2.3 pg/mL (ng/L) across the studies performed. The maximum observed LoD for Access hsTnI is 2.3 pg/mL (ng/L).

LIMIT OF QUANTITATION

Limit of Quantitation (LoQ) was tested using a protocol based on CLSI EP17-A2.[36] Studies were performed using a total of 3 reagent lots, 3 calibrator lots and multiple UniCel DxI 600 and 800 Access Immunoassay Systems. Serum and lithium heparin plasma samples were evaluated. In each study, 5 replicates of 13 samples were measured in 10 runs. LoQ was determined as the lowest concentration which met the design requirements of total imprecision ≤ 20% CV. The 20% CV LoQ for the Access hsTnI assay ranged from 1.2 to 2.3 pg/mL (ng/L) across the studies performed. The maximum observed 20% CV LoQ for Access hsTnI is 2.3 pg/mL (ng/L).

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STANDARD OPERATING POLICY AND PROCEDURE MANUAL

DXI 600/124 **High sensitivity Troponin I**

APPENDIX A– HUH HIGH SENSITIVITY TROPONIN ALGORITHM (REFERENCE RANGE)