

Date: January 29, 2018

To: Affiliated Laboratory Clients

RE: INTRODUCING THE NEW HIGH SENSITIVITY TROPONIN T ASSAY (TROPONIN T HS)

On 1/31/2018, Affiliated Laboratory, Inc. will replace the current 4th generation Troponin T assay with the 5th generation Troponin T assay (Elecsys Troponin T Gen 5 STAT). **This new assay is often referred to as a "high sensitivity" troponin assay for its ability to detect troponin values at or above the limit of detection in ≥50% of a reference ("normal") population.** Several key differences with this new assay include:

- Measurable values at or above the lower limit of detection in $\geq 50\%$ of a reference ("normal") population.
 - Since 50% of "normal" individuals will have detectable troponin, serial monitoring to detect rising or falling values (aka "dynamic" pattern) is *key* to proper interpretation of results.
- Extremely precise: coefficient of variation $\leq 10\%$ at the 99th percentile upper reference limit.
 - Values should not bounce around due to background analytical "noise".
- **Whole number reporting in ng/L:** measuring range is 6-10000 ng/L; values below 6 ng/L are reported as < 6 ng/L while values greater than 10000 are reported as >10000 ng/L.
- **Sex specific reference (normal) ranges** (as defined by the 99th percentile upper reference limit):
 - **Women:** ≤ 14 ng/L
 - **Men:** ≤ 22 ng/L

Values greater than the 99th percentile upper reference limit by sex will be "flagged" as abnormal. The first elevated value in a series will be considered a critical value according to our current critical values policy. To distinguish this assay from other cardiac troponin assays (still in use at other sites), the new assay will be reported as **"Troponin T HS"**. *The previous 4th generation Troponin T assay will no longer be available at EMMC.*

Multiple studies have demonstrated an increased sensitivity and better early discrimination of acute myocardial infarction (AMI) with "high sensitivity" assays compared with contemporary assays. This translates into an excellent negative predictive value and has allowed for a shortening of the period for "rule out" of AMI and initiation of treatment.

The Third Universal Definition of Myocardial Infarction (MI) has confirmed cardiac troponin (cTn) as the biomarker of choice. **Diagnosis of MI is made with acute changes in cTn concentrations with at least one serial sample above the 99th percentile upper reference limit (URL), *taken together* with evidence of myocardial ischemia (symptoms, ECG changes or imaging results).** To distinguish between acute and chronic cTn elevations, the Universal Definition of MI stresses the need for serial sampling to observe a rise and/or fall of cTn above the 99th percentile URL.

Troponin T is released during the process of myocyte necrosis. While cardiac specific, it is not specific for MI and detectable levels may be seen in other disease states that involve the heart muscle (e.g. arrhythmia, acute aortic syndrome, acute heart failure, hypertensive crisis, myocarditis, pericarditis, pulmonary embolism and Takotsubo cardiomyopathy). **As such, ACC/EHA/AHA guidelines and the Universal Definition of MI recommend serial sampling with a rise and/or fall in troponin to distinguish between acute and chronic elevations.** Markedly elevated values ($>5X$ URL) have a high ($>90\%$) positive predictive value for acute type 1 MI. ***Regardless of the etiology, however, elevated highly***

sensitive Troponin T values (dynamic or stable), should be considered high risk and are highly associated with increased morbidity and mortality.

A multidisciplinary team at EMMC (including representatives from cardiology, emergency medicine and laboratory medicine) has developed a diagnostic algorithm based upon the **0/3 hour rule-out algorithm** according to the 2015 European Society of Cardiology (ESC) guidelines. **To assist in the use and interpretation of this new assay and to allow for efficient cardiac rule-outs, we recommend that providers routinely follow this algorithm.** European experience has also demonstrated even earlier cardiac rule-outs using highly sensitive troponin assays, including 0/1 hour algorithms and rule outs based upon a single highly sensitive troponin value below the limit of detection at patient presentation. It is possible that these shorter rule outs will become commonplace in the U.S. in the not too distant future.

The new cardiac troponin T assay can be ordered as part of the chest pain biomarker (troponin) protocol which includes a baseline value, additional draw at 3 hours and a possible reflexed third draw at 6 hours depending upon the degree of change between the baseline and 3 hour value (aka "delta" value). The test may also be ordered on a random basis. This test is available 24/7 and requires a lithium heparin (light green top) tube.

The following interpretative comment will chart with each result:

“Results exceeding the upper reference limit (as defined by the 99th percentile by sex) indicate myocardial injury. While cardiac specific, troponins are not specific for myocardial infarction (MI) and elevated levels may be seen in other disease states that involve the heart muscle. ACC/ESC/AHA guidelines and the Universal Definition of MI recommend serial sampling to determine a rising and/or falling pattern to distinguish an acute ischemic etiology from other etiologies. Troponin results should always be used in conjunction with clinical signs and symptoms.

The International Federation of Clinical Chemistry (IFCC) defines a high-sensitivity troponin test as one that can measure cardiac troponin (cTn) above the Limit of Detection in $\geq 50\%$ of healthy subjects.”

If you have any questions or concerns, please do not hesitate to contact Dr. Buetens, laboratory medical director at 941-8200.

REFERENCES:

Elecsys Troponin T Gen 5 STAT package insert 2017-03 V1.0

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