Test Bulletin

ACL Laboratories
Every Sample is a Life™

November 2018

ACL Laboratories Revises General Requisition

Effective immediately, ACL Laboratories revised the general ACL test requisition.

Highlighted updates include:

- The top portion of the requisition is divided with patient data on the left and billing information on the right.
- "Other Tests, Special Instructions or Clinical History" custom section space has increased.
- ACL test order codes have been updated and some test names have been updated for further clarification.
- The revised requisition only has two copies: one for the client and one for the laboratory.

Please deplete your current ACL test requisition inventory before ordering new requisitions. For your patient's safety, ACL encourages clients to take advantage of electronic test ordering capabilities. Please contact your ACL Business Development representative or call ACL Client Services at 1.800.877.7016 to learn more about ordering your laboratory testing electronically.

CHANGE: Urine Chemistry Storage, Stability, and Transport

Effective Wednesday, November 14, 2018, ACL Laboratories will no longer accept samples stored at ambient (room) temperature for urine chemistry testing. This includes random, timed, and 24 hour urine specimens. The reason for this change is to maintain specimen integrity; whereby, enhancing the quality and accuracy of results. Urine specimens that are maintained at room temperature quickly deteriorate and results may then be adversely affected.

The following are examples of urine chemistry tests that will no longer be accepted if submitted at an ambient temperature:

Test	Test Order Code
Amylase	UAMY & UAMU
Beta 2 microglobulin	UB2M & UB2MU
Calcium	UCA & UCAU
Chloride	UCL & UCLU
Creatinine	UCR & UCREA & UCRL
Glucose	UGLUR & UGLUU
Magnesium	UMG & UMGU
Microalbumin	MAR, UMALB, & UMU
Osmolality	UOSM
Phosphorus	UPHOS & UPU
Potassium	UK & UKU
Sodium	UNA & UNAU
Total Protein	UTP & UTPU
Uric Acid	UUA & UUAU
Urea Nitrogen	UUN, UUNU & UUNCL
Protein/Creatinine Ratio	PCRR
Calcium/Creatinine Ratio	CACRR

For additional information regarding this test, as well as specimen collection requirements, please contact ACL Client Services at 1.800.877.7016 or visit our website at www.acllaboratories.com/test-catalog/.

ACL Laboratories Adds Toxin EIA Testing to C. *difficile* Testing Algorithm

Effective November 14, 2018 ACL Laboratories will change its testing approach for the identification of *Clostridioides (Clostridium) difficile*.

The current testing approach utilizes a molecular test to detect the presence of the C. *difficile* bacterium, but cannot differentiate between asymptomatic colonization and active infection, which often leads to overtreatment of patients. The new testing strategy will be an algorithmic approach that begins with the current molecular test. However, with the new algorithm all specimens testing positive in the molecular assay will now be reflexed to an enzyme immunoassay (EIA) that is designed to detect the actual toxin protein. The presence of this protein has a very strong correlation with active C. *difficile* disease and generally warrants treatment while the absence of this protein is often associated with colonization or milder disease that may not necessarily require treatment. Specimens testing negative for C. *difficile* in the molecular test will not be reflexed to the EIA assay.

The decision to update the C. *difficile* testing approach has been a collaborative effort between ACL Laboratories and the Advocate Aurora Health Infection Prevention and Antimicrobial Stewardship teams. This decision was largely based on the "Clinical Practice Guidelines for C. *difficile* Infection in Adults and Children" released in February 2018 by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). In addition, recent changes to the reporting criteria benefit hospitals utilizing this type of testing approach (compared to a molecular test alone) when reporting hospital acquired C. *difficile* infections to the National Healthcare Safety Network (NHSN).

The C. *difficile* test order name will remain the same as it is currently listed in hospital information systems, but will now contain the following two result components along with an interpretive comment:

C. *diff* Tox by PCR (this component is equivalent to the current test)
C. *diff* Tox by EIA (this is the new component indicative of the presence of actual toxin protein)

The two tests may not be ordered individually and the EIA test will automatically be performed on all specimens testing positive in the molecular assay. The results of the PCR test will be withheld until the EIA test is complete and both tests will be reported simultaneously. The toxin EIA test takes approximately 30 minutes to perform so results are not expected to take significantly longer to report than they currently do.

This table shows the new result format that will appear on patient charts:

C. *diff* Tox by PCR	C. *diff* Tox by EIA	The following comment will append…
Not Detected	Testing Not Indicated	C. *difficile* infection is highly unlikely. Submission of additional specimens within 7 days is not recommended
Detected	Not Detected*	Clinical evaluation is necessary and alternative causes of diarrhea should be ruled out. Test results may represent C. *difficile* colonization or infection with a lower burden of disease. Most patients who are toxin EIA negative improve without treatment, but if clinical suspicion is high for C. *difficile* infection, treatment may be considered.
Detected	Detected*	Toxigenic C. *difficile* detected, which indicates a high likelihood of active infection. Submission of additional specimens within 14 days is not recommended.

*Note that additional charges will be necessary for a final test result.

Please contact ACL Client Services at 1.800.877.7016 with any questions regarding this new testing approach.

NT proBNP, Frequently Asked Questions

Effective August 15, 2018, ACL Laboratories implemented testing for NT proBNP (N-terminal pro b-type natriuretic peptide) as a replacement for BNP (B-type natriuretic peptide).

1. Why did ACL choose to move from BNP testing to NT proBNP?

Recent clinical evidence suggests that NT proBNP is a superior marker of heart failure compared to BNP in the diagnosis, prognosis, and management of heart failure. The advantages of NT proBNP include greater sensitivity for the detection of chronic heart failure. NT proBNP has also been used in the risk stratification of patients with acute coronary syndrome and as an aid in the assessment of increased risk of cardiovascular events and mortality in patients in patients at risk for heart failure who have stable coronary artery disease.

2. What are the differences between BNP and NT proBNP?

BNP and NT proBNP are two different biochemical markers with different characteristics. The rise of NT proBNP in response to myocardial stress is often several orders of magnitude higher than BNP. NT proBNP levels tend to be significantly higher than BNP for a given condition. In addition, the half-life of NT proBNP is longer compared to BNP (120 minutes vs 20 minutes). These characteristics contribute to greater analytical stability, accuracy, and precision of the assay. In addition, a major clinical advantage of NT proBNP over BNP is that levels are NOT affected by current heart failure treatment regimens such as Entresto treatment.

3. Why is the reference range different for NT ProBNP vs BNP?

The two markers are different biochemically and results obtained with NT proBNP and BNP assays are NOT equivalent and blood concentrations can vary greatly between the two assays. Plasma concentrations of NT proBNP are higher in older individuals. In addition there have been reported gender and body mass index differences as well. The established reference range (Expected value in normal subjects) is:

<75 years: <126 pg/mL
≥75 years: <451 pg/mL

The optimal value for distinguishing heart failure from other causes of dyspnea varies with patient age. For patients <50, 50 to 75, and >75 years of age, the optimal plasma NT proBNP cutoffs for diagnosing Heart failure are 450 pg/mL, 900 pg/mL, and 1800 pg/mL respectively. Overall, these cutoffs yield a sensitivity and specificity of 90 and 84 percent, respectively. In addition, NT proBNP increases with renal failure and optimal cut-off values for diagnosis in such patients have not been clearly established. (See Question 5 below)

4. Can BNP and NT proBNP results be compared to each other?

Results obtained with NT proBNP and BNP assays are NOT equivalent and blood concentrations can vary greatly; therefore, results obtained with NT proBNP and BNP cannot be compared or interchanged. In many patients NT proBNP concentrations can be 8-10 fold higher than BNP levels due to the sensitivity of the marker. There is limited data available comparing the diagnostic and prognostic values of plasma BNP and NT proBNP and there is no universal conversion factor that can be used. Of importance is an elevated value based on the established reference range (the range of "normal" patients) and diagnostic cut-offs (the level at which clinical interventions occur).

5. How are NTproBNP levels affected by renal dysfunction?

In patients with chronic kidney disease, decreased estimated GFR is associated with an increase in both BNP and even greater elevation in NT proBNP concentrations, even in the absence of clinically diagnosed heart failure. NT proBNP is cleared by the kidney and its plasma concentration can be elevated by renal failure alone, in the absence of heart disease. There is insufficient data to establish clear cut-off values for NT proBNP in this setting. Recent literature suggests a diagnostic cut-off in patients with a serum creatinine ≤2.5 mg/dL and an estimated glomerular filtration rate (GFR) of ≥60 mL/min per 1.73 m^2 as >450 pg/mL in those less than 50 years of age and >900 pg/mL in older patients. A cut-off of 1,200 pg/mL has been suggested in patients with a GFR <60 mL/min per 1.73 m^2. The main value of NT proBNP would be the finding of a normal NT proBNP in these patients, which would exclude left ventricular dysfunction.

NT proBNP, Frequently Asked Questions, continued

6. Is there value to repeated or serial measurements of NT proBNP?

A single elevated NT proBNP is a strong indication of heart failure in the absence of renal dysfunction. Higher levels of NT proBNP are associated with disease severity and the risk of heart failure. Recently, there is increasing evidence that serial measurements of NT proBNP may be beneficial for further risk stratification and treatment monitoring in patients with chronic heart disease. One study showed that a reduction of NT proBNP levels after 1 month was associated with improved outcome. In addition, NT proBNP levels are useful in monitoring the effectiveness of Entresto treatment in patients with chronic heart disease. A reduction in NT proBNP levels post treatment is associated with improved outcome and prognosis.

Digoxin Specimen Collection/Draw Time

Patient Safety issues related to the timing of draws for digoxin levels have been reported multiple times from several sources over the years. After oral administration, there is an early rise in serum digoxin concentration. It takes approximately 6 to 8 hours post oral dose before equilibration of serum and tissue levels occur. Therefore, for therapeutic monitoring the sample should be collected at least 6 to 8 hours after the last dose. When a sample for digoxin is drawn prior to this time the result is not interpretable. Due to the narrow therapeutic range of digoxin, small variations in blood concentration may result in toxic or sub therapeutic concentrations, making the timing even more critical.

If the time of the dose relative to the time of blood draw is not correct or is unknown, toxicity may be falsely assumed. Some patients have been called to immediately report for treatment related to digoxin toxicity when later it is found that the sample was incorrectly drawn too early after the last dose, thus making it appear that the level was in the toxic range.

It is acknowledged that patient education by the provider regarding the timing of the blood draw and then patient compliance with those instructions are ideal; however, this does not consistently occur. The laboratory has been asked to intervene to help ensure that the blood draw is appropriately aligned with the last dose of medication.

Below is the process that will be implemented starting **Wednesday, November 14, 2018.**

Inpatients

- The hospital computer systems will have a standard comment that will remind the viewer that digoxin blood samples must be drawn at least 6 hours post dose.
- A computer generated comment will require the phlebotomist to check with the nurse prior to drawing a sample for digoxin to confirm it has been at least 6 hours since the last dose. If it has not met this timeframe, the phlebotomist will return for the blood draw at the appropriate time.
- The time of collection will be entered into computer system as per standard practice.

Outpatients/Outreach

- If an outpatient presents for a digoxin blood draw and it is confirmed that it has not been at least 6 hours post dose, the patient may choose to remain until the appropriate time frame is met or choose to return at the appropriate time.
- If the patient chooses to return later, a cancellation of the order will occur along with a comment entered that states: "Sample was not obtained due to inadequate number of hours since last dose, patient instructed to return at least 6 hours post dose".
- A request for a new order will be sent to the ordering provider.
- The time of collection will be entered into the computer system as per standard practice.

ACL Laboratories Offers New Quantitative Pain Management Drug Testing Panel

Effective Wednesday, November 14, 2018, ACL Laboratories will offer a new test, Pain Management Profile 1 (Test Order Code QPNMG1).

This comprehensive drug screen is intended for use in the management of pain management patients and those requiring routine drug monitoring. This panel utilizes both immunoassay screening methods as well as definitive LC/MS methods to screen for common prescribed and abused drugs. All positive immunoassay results will auto-reflex to definitive LC/MS testing. All positive results will be quantitatively reported.

Patient medication information must be provided to receive an interpretative report. Results will indicate whether findings are consistent or inconsistent with supplied medication information.

Specimen Collection	30 mL Random Urine
Sample Handling	Specimen must be received in a sterile urine cup. Do not transfer to an aliquot tube
Sample Transport	Refrigerated
Test Performance	Monday – Saturday
Turnaround Time	Within 5 days
CPT Code	80307

The following drugs/classes of drugs will be screened and ALL positive results will auto-reflex to definitive LC/MS confirmation:

	Positive Cut-off
Amphetamine/Metamphetamine	500 ng/mL
Barbiturates	300 ng/mL
Buprenorphine/Naloxone	5 ng/mL
Cocaine Metabolite (Benzoylecgonine)	150 ng/mL
Fentanyl	0.5 ng/mL
Heroin Metabolite (6-Acetylmorphine)	10 ng/mL
Marijuana Metabolite (THC)	20 ng/mL
MDMA/MDA	500 ng/mL
Methadone	100 ng/mL
Phencyclidine	25 ng/mL
Propoxyphene	300 ng/mL

ACL Laboratories Offers New Quantitative Pain Management Drug Testing Panel, continued

The following drugs will be tested definitively by LC/MS and all values above the cut-off concentration quantitatively reported:

	Positive Cut-off
Gabapentin	1,000 ng/mL
Meperidine & Normeperidine	100 ng/mL
Meprobamate (Carisoprodol metabolite)	1,000 ng/mL
Pregabalin	1,000 ng/mL
Tapentadol & Nortapentadol	50 ng/mL
Tramadol & Desmethyltramadol	100 ng/mL
Benzodiazepines, Quantitation	
Alphahydroxyalprazolam	25 ng/mL
Alphahydroxymidazolam	50 ng/mL
Alphahydroxytriazolam	50 ng/mL
Aminoclonazepam	25 ng/mL
Hydroxyethlyflurazepam	50 ng/mL
Lorazepam	50 ng/mL
Nordiazepam	50 ng/mL
Oxazepam	50 ng/mL
Temazepam	50 ng/mL
Opiates, Expanded Quantitation	
Codeine	50 ng/mL
Hydrocodone	50 ng/mL
Hydromorphone	50 ng/mL
Morphine	50 ng/mL
Norhydrocodone	50 ng/mL
Noroxycodone	50 ng/mL
Oxycodone	50 ng/mL
Oxymorphone	50 ng/mL

For additional information regarding these tests, as well as specimen collection requirements, please visit ACL Laboratories Directory of Services at http://www.acllaboratories.com/test-catalog/ or contact ACL Client Services at 1.800.877.7016.