MEMORANDUM

To: OSF System Lab clients and partners

From: James Siebert, M.D. – Laboratory Medical Director

Subject: Anti-Neutrophil Cytoplasmic Antibody (ANCA) & Glomerular Basement Membrane (GBM) Testing

Date: October 27, 2016

Effective November 28, 2016, the OSF System Laboratory will be making changes in the tests for Anti-Neutrophil Cytoplasmic Antibodies (ANCA) and Glomerular Basement Membrane (GBM) Antibodies. Myeloperoxidase (MPO) and Proteinase 3 (PR3) IgG autoantibody testing currently performed by ELISA, as well as GBM testing will now be performed on the BioPlex® 2200 multiplex flow cytometry platform (Bio-Rad Laboratories, Hercules, CA, USA). MPO and PR3 will be incorporated into a comprehensive ANCA screening panel on the BioPlex® 2200 (LAB1894). The BioPlex® 2200 is a fully automated Luminex-based system developed for high-throughput simultaneous analysis of autoimmune analytes in a single tube. The advantages of the BioPlex include a shorter turnaround time, detection of multiple antibodies simultaneously, less inter-observer variability, and less phlebotomy for patients.

The new BioPlex panel offers semi-quantitative detection of specific antibodies directed to the underlying disease process in patients with vasculitis: Myeloperoxidase (MPO) and Proteinase 3 (PR3) IgG autoantibodies. Anti-PR3 and anti-MPO antibodies are 90% sensitive in detecting small vessel vasculitis (a negative test does not exclude vasculitis).\(^1\) C-ANCA is associated with anti-PR3 antibodies and is found in Wegener’s Granulomatosis (Granulomatosis with Polyangiitis), and Churg-Strauss Syndrome (Eosinophilic Granulomatosis with Polyangiitis). P-ANCA is associated with anti-MPO antibodies and is found in Microscopic Polyangiitis, Crescentic Glomerulonephritis and Churg-Strauss Syndrome. However, there is variability within this antibody panel: a positive ANCA with negative anti-MPO and PR3 may be found in a variety of conditions, including autoimmune hepatitis, sclerosing cholangitis, ulcerative colitis, SLE, RA, and chronic infections. ANCA assays still be reported as a Perinuclear or Cytoplasmic pattern when a positive IFA is observed.

<table>
<thead>
<tr>
<th>ANTIBODY</th>
<th>Test Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANCA screening panel (anti-MPO; anti-PR3; ANCA)</td>
<td>LAB1894</td>
</tr>
<tr>
<td>Glomerular Basement Membrane (anti-GBM)</td>
<td>LAB4613</td>
</tr>
<tr>
<td>Myeloperoxidase Ab (anti-MPO)</td>
<td>LAB1890</td>
</tr>
<tr>
<td>Proteinase 3 Ab (anti-PR3)</td>
<td>LAB1892</td>
</tr>
</tbody>
</table>

Table 1. ANCA and GBM test options and corresponding LAB test codes
The ANCA panel on the BioPlex® 2200 is an excellent screening test for vasculitis, with a high level of diagnostic accuracy and more rapid and consistent results than IFA based serologies.¹

Table 2. ANCA & GBM tests slated to be inactivated:
LAB1891: ANCA Antibodies: MPO and PR3
LAB1903: Glomerular Basement Membrane Antibodies IgG, GBM (currently sent to Mayo Medical Laboratory)

Glomerular Basement Membrane antibody testing will also transition to BioPlex. Antibodies to GBM are primarily directed towards the non-collagenous domain of type IV collagen. Antibodies directed against collagen found in glomeruli and alveoli is associated with rapidly progressive glomerulonephritis and alveolitis (Goodpasture’s Syndrome). Anti-GBM may also be found in some patients with ANCA positive small vessel vasculitis, usually with anti-MPO antibodies. Since, anti-collagen antibody is detected by the BioPlex® 2200 with a high degree of sensitivity and specificity, the BioPlex system will provide excellent discrimination for these overlapping clinical entities.

Patients with a history of vasculitis may continue to be followed with serial IFA (Indirect Fluorescent Antibody) ANCA tests as in the past with the current ANCA, screen and titer if positive / ANCA titer and pattern (LAB1893 & LAB1896, respectively). Patients undergoing successful therapy for an autoimmune disorder may be negative for ANCA by these methods.

Any questions or concerns may be addressed to your OSF clinical client representative or to:

John Farrell, MD – Medical Director of Clinical Microbiology & Serology Labs
OSF System Laboratory
(309) 624-9127