OSF
SYSTEM LABORATORY

MEMORANDUM

To: OSF System Lab Partners & Clients

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

Subject: **Celiac screening / Celiac Serology**

Date: October 18, 2016

In the near future (implementation date TBD), the OSF System Laboratory will move from serologic testing for Celiac disease by enzyme linked immunosorbent assay (ELISA) to performing Celiac serology in the OSF System Lab on the BioPlex® 2200 multiplex flow cytometry platform (Bio-Rad Laboratories, Hercules, CA, USA) as the initial screening test for diagnosis of Celiac disease. Since this is an automated platform with direct throughput, the turnaround time for celiac testing will be substantially improved.

Diagnosis of celiac disease (CD) is primarily based on the constellation of clinical and family history, serology testing (while on a gluten containing diet), and small bowel biopsy. Serologic tests are categorized as either IgA or IgG. Immunoglobulin A (IgA) anti-tissue transglutaminase (tTG) antibody is the preferred initial test for detection of CD as well as monitoring response to treatment.[1] The sensitivity of the tTG-IgA for untreated CD is 95%, with a specificity $\geq$ 95%.[2,3] In patients in whom low IgA or selective IgA deficiency (IgAD) is identified, IgG-based testing should be performed. Combining tests for CD in lieu of tTG IgA alone may marginally increase the sensitivity for CD, but reduces specificity and is not recommended in low-risk populations.[1]

The BioPlex® 2200 uses Luminex™ methodology to provide simultaneous measurement of anti-tTG and deamidated gliadin peptide (DGP) IgA antibody levels using a fully automated random access analyzer. The flow cytometer also employs an IgA Verification Bead (AVB) to check for IgAD to ensure that IgAD patients are identified and tested accordingly, with IgG based assays. The BioPlex platform will improve the turnaround time for CD test results, and patient satisfaction will also improve, since multiple tubes of blood will not be required to screen for CD and IgAD.

The test code for the new **Celiac Panel with reflex** on the BioPlex® 2200 is **LAB 1850**. Because this new multiplex flow-cytometry platform includes tTG IgA, DGP IgA, with a total IgA test (immunoturbidimetric assay) driving a reflex to tTG IgG and DGP IgG when the total IgA (immunoturbidimetric) is decreased, the following equivalent tests will be removed from electronic order options:

LAB821: Prometheus Celiac Serology
LAB820: Prometheus Celiac Genetics
LAB856: Prometheus Celiac PLUS
LAB2209: Mayo Celiac Disease Serology Cascade
LAB2210: Mayo Celiac Disease Comprehensive Cascade
LAB2213: Mayo Transglutaminase (tTG) Antibody, IgG

HLA heredity plays a role in CD (*e.g.*, HLA-DQ2 and HLA-DQ8 increase one's predisposition to CD). When the results of serologic and endoscopic testing are equivocal, although HLA typing is not required to establish a diagnosis of celiac disease, since additional serologic testing is rarely illuminating, testing for HLA-DQ2 and HLA-DQ8 (LAB820 MAYO test Code) could be considered. Anti-endomysial (EMA) IgA assays have similar sensitivity and specificity to TTG IgA assays (see Table 1) and are not included in the BioPlex Celiac screening panel.

Table 1. Diagnostic Tests for Celiac Disease[3-5]

			Likelihood ratio (LR)
SEROLOGIC TESTS**	**Sensitivity**	**Specificity**	**LR +**
IgA tissue transglutaminase (tTG) Ab	95 – 98**%**	95%	17.5
IgA deamidated gliadin peptide (DGP) Ab	88%	95%	17.5
IgG tissue transglutaminase (tTG) Ab	40%	95%	8
IgG deamidated gliadin peptide (DGP) Ab	80%	98%	40
IgA endomysial antibody	90%	95%	18

******tTG IgA, DGP IgA, tTG IgG, and DGP IgG are all included in the BioPlex® 2200 Celiac Panel

Any questions or concerns should be addressed to your assigned client representative or to:

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

1. Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA. Diagnosis and Management of Celiac Disease. Am J Gastroenterol 2013; 108:656–676.
2. Book L, Zone JJ, Neuhausen SL. Prevalence of celiac disease among relatives of sib pairs with celiac disease in U.S. families. Am J Gastroenterol 2003;98:377–381.
3. Lewis NR, Scott BB. Meta-analysis: deamidated gliadin peptide antibody and tissue transglutaminase antibody compared as screening tests for coeliac disease. Aliment Pharmacol Ther 2010;31:73–81.
4. Leffler DA, Schuppan D. Update on serologic testing in celiac disease. Am J Gastroenterol. 2010;105:2520-2524.
5. Reddick BK, Crowell K, Fu B. Clinical inquiries: What blood tests help diagnose celiac disease? J Fam Pract. 2006;55(12):1088- 93.

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Symptomatic Individuals:
-Non-specific symptoms (anemia, diarrhea, failure to thrive, fever, skin rash and weight loss)
-Diarrhea more than 4 weeks duration

Indications for testing

Asymptomatic Individuals with:
-Celiac disease in first-degree relatives
-Autoimmune disease associated with celiac disease (diabetes mellitus type 1, autoimmune thyroiditis, etc.)
-Non-autoimmune conditions associated with celiac disease (Down Syndrome, Turner Syndrome, etc.)
-Early-onset osteoporosis

ORDER
Celiac Panel with Reflex LAB1850
Includes:
Tissue Transglutaminase (tTG) IgA
Deamidated Gliadin IgA
Immunoglobulin IgA
Above 3 components can be ordered individually

Normal Total IgA

IgA below age matched values

Result interpretation of Tissue Transglutaminase (tTG) IgA Deamidated Gliadin IgA

tTG IgA >= 15 units, highly suggestive of celiac disease

Either result positive

Automatic reflex to: Tissue Transglutaminase (tTG) IgG Deamidated Gliadin IgG

All results normal

Confirm with small intestine biopsy

Positive

Celiac disease

If both tTG IgA and d-gliadin IgA <15 units, celiac disease very unlikely.

Negative

=10% of patients with celiac disease are seronegative. If celiac disease is suspected, consider Celiac-associated HLA-DQ Alpha 1 and DQ Beta 1 DNA Typing, Mayo CELI LAB2208

Negative

Not celiac disease

Positive

Positive

=10% of patients with celiac disease are seronegative. If celiac disease is suspected, consider Celiac-associated HLA-DQ Alpha 1 and DQ Beta 1 DNA Typing, Mayo CELI LAB2208

Negative

Not celiac disease

Positive

Possible celiac disease. Follow-up with patient for future development of celiac disease

Biopsy results inconsistent with serology. Consider Celiac-associated HLA-DQ Alpha 1 and DQ Beta 1 DNA Typing, Mayo CELI LAB2208

Negative

Not celiac disease

Positive

Possible celiac disease. Follow-up with patient for future development of celiac disease