

# **Reflex Testing**

Corewell Health West

## **Contents**

|   |    |
|---|----|
| <b>Anatomical Pathology</b> .....                           | 2  |
| <b>Chemistry Reflex Testing</b> .....                       | 5  |
| <b>Coagulation Reflex Testing</b> .....                     | 6  |
| <b>Cytogenetics Reflex Testing</b> .....                    | 7  |
| <b>Cytology Reflex Testing</b> .....                        | 8  |
| <b>Flow Cytometry Reflex Testing</b> .....                  | 9  |
| <b>Hematology Reflex Testing</b> .....                      | 10 |
| <b>Hematopathology Reflex Testing</b> .....                 | 11 |
| <b>Immunochemistry Reflex Testing</b> .....                 | 12 |
| <b>Microbiology Reflex Testing</b> .....                    | 14 |
| <b>Molecular Diagnostics Reflex Testing</b> .....           | 15 |
| <b>Referrals Reflex Testing</b> .....                       | 16 |
| <b>Toxicology Reflex Testing</b> .....                      | 17 |
| <b>Transfusion Medicine/Blood Bank Reflex Testing</b> ..... | 18 |
| <b>Urinalysis Reflex Testing</b> .....                      | 19 |

\*Changes highlighted are approved in current calendar year, highlighting will be removed in subsequent calendar year.

\*Under certain circumstances reflex testing may be initiated based on NCCN guidelines, see MEC form (07/13/2020) for more details.

## Anatomical Pathology

| <b>Anatomic Pathology – Mandatory</b>  |   |
|--|---|
| Initial Test and Result  | Confirmation Testing/Additional Workup  |
| <b>Brain</b>   |   |
| Brain – high grade gliomas   | MGMT Methylation Analysis   |
| <b>Breast</b>  |   |
| <p>All patients with invasive breast carcinoma meeting the following criteria:</p> <ul style="list-style-type: none"> <li>Age less than 70 years</li> <li>Not pure tubular, mucinous, or colloid carcinoma (grade 1 special subtypes with good prognosis)</li> <li>Tumor is pathologic stage pT1b, T1c, T2, or T3</li> <li>Tumor is pathologic stage pN0 or N1mi</li> <li>Tumor is ER positive and Her2/neu negative</li> </ul> <p>Not post-treatment (y), recurrent tumor (r) or with known distant metastatic tumor (M1)</p> | <p>Send for Oncotype DX testing:</p> <ol style="list-style-type: none"> <li>1) If multifocal on same side and meet the criteria               <ul style="list-style-type: none"> <li>Perform Oncotype on largest primary tumor (if same histology)</li> <li>Perform Oncotype on up to three primary tumors (if different histology), indicate order of testing to Oncotype (as they will stop further testing if high recurrence score is resulted)</li> </ul> </li> <li>2) If bilateral, perform Oncotype on both sides if meet the criteria.</li> </ol> <p>If the patient has a different higher risk concurrent breast cancer such pT4, pN1b or more, ER negative, or Her2, do not reflexively test any additional lower risk tumor(s). The higher risk cancer will drive the patient's treatment and prognosis so testing the lower risk one is not done as reflex.</p> |
| <p>Primary and recurrent/metastatic Invasive Mammary Carcinoma (excisional biopsy / lumpectomy / mastectomy)</p> <p style="text-align: right; color: yellow; font-weight: bold;">As per NCCN Guidelines 2024</p>   | <p>Immunohistochemical stains for estrogen, progesterone, and Her2</p>  |
| <p>Ductal Carcinoma In Situ (DCIS)</p> <p style="text-align: right; color: yellow; font-weight: bold;">As per NCCN Guidelines 2024</p>   | <p>Immunohistochemical stains for estrogen and progesterone</p>   |
| <b>GI (Gastrointestinal)</b>   |   |
| <p>Metastatic gastrointestinal tract adenocarcinomas (gastric, esophageal, small bowel, colon and rectum)</p> <p style="text-align: right; color: gray; font-weight: normal;">As per NCCN guidelines 2022</p>  | <ul style="list-style-type: none"> <li>Perform Her2/neu immunohistochemistry (IHC). When metastasis is pathologically confirmed (can use either metastatic site or primary tumor), or highly suspicious for metastatic disease on imaging.</li> </ul> <p>Equivocal IHC results will reflex to HER2 FISH testing</p> <ul style="list-style-type: none"> <li>Perform MMR evaluation (Immunohistochemical protein studies for MSH2, MSH6, MLH1, PMS2), if previously not performed on main tumor</li> </ul> <p>Based on MMR results reflex to additional testing as per current CAP protocol</p>   |

| <b>Anatomic Pathology – Mandatory</b>  |   |
|--|---|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>   |
| Metastatic Colorectal Carcinoma  | Colon Mutation Analysis Panel<br><br>-includes genotyping for KRAS, NRAS, and BRAF mutations  |
| All newly diagnosed gastrointestinal tract (luminal) adenocarcinomas (gastric, esophageal, small bowel, colon and rectum)<br><br>As per NCCN guidelines 2022   | <ul style="list-style-type: none"> <li>Immunohistochemical (IHC) protein studies for MSH2, MSH6, MLH1, PMS2</li> </ul> Based on MMR results reflex to additional testing as per current CAP protocol  |
| Gastric (stomach) gastrointestinal stromal tumors (GISTs) with epithelioid morphology<br><br>As per NCCN guidelines 2022   | <ul style="list-style-type: none"> <li>SHDB immunohistochemical stain</li> </ul>  |
| <b>GYN (Gynecological)</b>   |   |
| All newly diagnosed or previously untested Adult Granulosa Cell Tumors, Serous Borderline Tumors, and Low-Grade Serous Carcinomas  | IHC for Estrogen and Progesterone receptors   |
| GYN sentinel lymph nodes which show no evidence of metastasis on initial H&E levels (applies to all GYN sentinel lymph nodes, including, but not limited to, those removed for endometrial, vulvar, and cervical carcinomas).  | Cytokeratin AE1/AE3 (to be performed on all blocks of all nodes deemed negative for metastasis following initial review of H&E sections).   |
| All newly diagnosed patients with endometrial cancer, including carcinosarcoma, and including cases of recurrence when no IHC was previously performed<br><br>November 2024  | MSH2, MSH6, MLH1, PMS2<br>Based on MMR results reflex to additional testing as per current CAP protocol<br>- Estrogen receptor<br>- p53<br>- If serous carcinoma or carcinosarcoma/MMMT: also order HER2 with reflex FISH for equivocal IHC |
| All FIGO <u>stage 1 and 2</u> (ie. Confined to uterus and cervix, see below highlighted) EXCEPT those that are<br><br><ul style="list-style-type: none"> <li>Stage 1a (no or &lt;50% invasion)</li> <li>AND grade 1/2 endometrioid adenocarcinoma</li> <li>AND p53 normal with absent or minimal lymphovascular invasion</li> </ul> May 2023 | POLE molecular testing (an in-house molecular test)   |
| <b>Head &amp; Neck</b>   |   |
| All newly diagnosed or previously untested oropharyngeal squamous cell carcinomas  | p16 immunohistochemistry (surrogate marker for HPV)   |

| <b>Anatomic Pathology – Mandatory</b>  |  |
|--|--|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>                                  |
| <b>Lung</b>  |  |
| Stage 4 lung non-small cell carcinoma (both adenocarcinoma and squamous cell carcinoma)<br><br>As per NCCN guidelines 2024   | PD-L1 and lung molecular panel   |
| Lymph node biopsy/cytology positive for non-small cell carcinoma (both adenocarcinoma and squamous cell carcinoma)<br><br>As per NCCN guidelines 2024  | PD-L1, and molecular testing for EGFR and ALK                                  |
| Rection cases of non-small cell carcinoma (both adenocarcinoma and squamous cell carcinoma) which show<br>- Tumor size 4 cm or greater, or positive lymph node(s)<br><br>As per NCCN guidelines 2024 | PD-L1, and molecular testing for EGFR and ALK                                  |
| <b>Melanoma</b>  |  |
| Metastatic melanoma Including cases with positive lymph nodes  | BRAF V600E IHC<br>- If IHC is negative reflex to <i>BRAF</i> molecular testing |
| <b>Other</b>   |  |
| Her2/neu immunohistochemistry equivocal (score 2+)   | Her-2/neu (ERBB2) Amplification by FISH  |

## Chemistry Reflex Testing

| <b>Chemistry – Mandatory</b>  |   |
|---|---|
| <b>Initial Test and Result</b>  | <b>Confirmation Testing/Additional Workup</b>   |
| HIV Quick Test (LAB175) performed at Corewell Health Reference Laboratory West  | If Reactive, reflex to HIV 1/HIV 2 Ab Ag Diagnostic (Roche) to be performed at Corewell Health Reference Laboratory West.   |
| HIV Quick Test (LAB175) ordered at Corewell Health Reference Laboratory West  | The HIV Quick Test is cancelled and reordered as HIV 1/HIV 2 Ab Ag Diagnostic (Roche). <i>(The Alere HIV Quick Test is not available at the Corewell Health Reference Laboratory West)</i>    |
| HIV 1/HIV 2 Ab Ag Diagnostic (Roche)  | If Reactive, reflex to Geenius HIV 1/HIV 2 Antibody Confirmation  |
| Reactive Hepatitis B surface antigen  | HbsAg Confirmation test   |
| Prostate Specific Antigen (PSA) Free Level  | PSA total on all orders that do not already have a PSA ordered on the same specimen.  |
| Reactive Syphilis IgG Antibody  | RPR titer at Corewell Health. If RPR is negative, additional TP-PA testing will be performed by MDHHS   |
| Random urine microalbumin   | Urine creatinine  |
| Thyroglobulin   | Automatically cancel AntiTgAB request when ordered with srTg  |
| Reactive Hepatitis C Virus Antibody   | HCV RNA   |
| <b>Chemistry – Optional</b>   |   |
| <b>Initial Test &amp; Result</b>  | <b>Optional Follow up Testing</b>   |
| <b>Lipid Panel do LDL Direct if Triglycerides &gt;400</b><br>Triglyceride result > 400 mg/dL  | LDL Direct  |
| <b>Preg Serum Quant Progesterone if</b><br>HCG result > 5 mIU/mL  | Progesterone level  |
| <b>PSA Sym FPSA if</b><br>PSA result between 2.5 and 10.0 ng/mL   | Free PSA  |
| <b>Thyroid Function Cascade</b><br>TSH result above 5.0 mcU/mL <b>or</b><br>TSH result below 0.3 mcU/mL <b>or</b><br>TSH result below 0.1 mcU/mL and FT4 result below 1.6 ng/dL | FT4 and TPO if TSH is above 5.0 mcU/mL<br>FT4 if TSH is below 0.3 mcU/mL<br><ul style="list-style-type: none"> <li>• Free T3 if TSH is below 0.1 mcU/mL and FT4 is below 1.6 ng/dL</li> </ul> |
| <b>TSH, Free T4 if indicated</b><br>TSH result above 5.0 mcU/mL <b>or</b><br>TSH result below 0.3 mcU/mL  | Free T4   |

## Coagulation Reflex Testing

| <b>Coagulation – Mandatory</b>   |   |
|--|---|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>   |
| aPTT with no endpoint detected or error code on the coagulation analyzer that cannot be resolved.                                    | Unfractionated Heparin  |
| Mixing Studies, aPTT, which does not correct   | Lupus Anticoagulant Screen (LA1)  |
| Mixing Studies, aPTT   | Heparin Neutralization (to rule out anticoagulant): <ul style="list-style-type: none"> <li>• If aPTT corrects to normal, then a Mixing Study is not indicated.</li> <li>• If aPTT remains elevated, then Unfractionated Heparin Level (anti-Xa assay) is ordered.</li> </ul> If Unfractionated Heparin Level is greater than 1.0 U/mL, then aPTT Mixing Study is not indicated. |
| Mixing Studies, PT, which does not correct   | Lupus Anticoagulant Screen (LA1)  |
| Factor activity testing showing non-parallelism inhibitor type pattern on serial dilutions<br><small>MEC Approved April 2022</small> | Lupus Screen  |
| Factor 8 Activity for patients on emicizumab (Hemlibra) recombinant factor 8 therapy   | Chromogenic Factor 8 Activity   |
| Heparin Dependent Antibody (HIT) Positive or Borderline  | Serotonin Release Assay (SRA)   |
| Lupus Screen LA1 elevated  | Perform LA2<br>Perform PT and aPTT <ul style="list-style-type: none"> <li>• If PT is elevated <math>\geq 4</math> seconds above normal range, perform PT mixing study</li> <li>• If aPTT is elevated <math>\geq 6</math> seconds above normal range, perform aPTT mixing study</li> </ul> Pathologist interpretation  |
| Platelet Aggregation Studies   | Platelet Count and hematocrit   |
| Platelet Function Assay (PFA 100) with Collagen/Epinephrine cartridge results greater than 180 seconds.                              | Collagen/ADP test   |
| Platelet Function Assay (PFA 100)  | Platelet Count and hematocrit   |

## Cytogenetics Reflex Testing

| <b>Cytogenetics - Mandatory</b>  |   |
|--|---|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>   |
| Bone Marrow samples with clinical indications for possible need to perform FISH Multiple Myeloma Panel   | Sort CD138 to purify (concentrate) sample and hold for possible FISH Multiple Myeloma Panel   |
| Multiple Myeloma Panel: If positive for IGH rearrangement<br><br>Updated by Lab February 2024  | Add t(11;14) IGH/CCND1<br>If negative for t(11;14) IGH/CCND1 add t(4;14) IGH/FGFR3 and t(14;16) IGH/MAF   |
| DLBCL Panel: If positive for MYC rearrangement ONLY<br><br>February 2024   | Add t(8;14) IGH/MYC/CEP8  |
| DLBCL Panel: If positive for BCL2 with or without BCL6 rearrangement and without MYC rearrangement<br><br>February 2024  | Add t(14;18) IGH/BCL2 dual fusion   |
| Chromosome Analysis Hematologic or Neoplastic Study<br><br>MEC Approved October 2022   | Chromosomal Microarray – Oncology (aCGH-Hematologic)  |
| Constitutional chromosome analysis, mosaic orders WITHOUT indications of Turner Syndrome, short stature, amenorrhea, or any indication associated with an increased risk of mosaicism<br><br>February 2024 | Routine constitutional chromosome analysis will be ordered in place of the mosaic order   |
| Chromosome studies with an indication of Turner Syndrome, short stature, amenorrhea, or any indication with possible mosaicism<br><br>Previously approved- added 2/2023                                    | PB Mosaic (30 cell analysis)  |
| Additional cell lines in chromosome study<br><br>Previously approved- added 2/2023   | Additional karyotype will be created to represent each addition cell line identified  |
| Abnormal or ambiguous microarray results<br><br>Previously approved- added 2/2023  | May be confirmed by cytogenetic chromosome analysis or fluorescence in situ hybridization (FISH) analysis as appropriate, based on specific abnormality, size and location of region identified |
| Newborn fluorescence in situ hybridization (FISH) studies<br><br>Previously approved- added 2/2023   | Cytogenetic chromosome analysis as appropriate with abnormal results on interphase FISH testing to fully characterize the abnormality identified  |

## Cytology Reflex Testing

| <b>Cytology - Mandatory</b>  |   |
|--|---|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>   |
| Pap test and HPV   | <p>Reflex Information</p> <p>Is HPV Requested?</p> <p>a. If NO HPV testing is desired, select NO and only the pap test will be ordered.</p> <p>b. If YES, HPV testing is desired, select one of two options:</p> <p>i. CO-TESTING (30-64 y/o)</p> <p>1. If Co-testing is selected, the HPV test will be ordered and performed regardless of the pap test final diagnosis.</p> <p>2. Note: Co-testing is recommended for patients age 30-64.</p> <p>ii. HPV REFLEX (see link below for criteria)</p> <p>1. If reflex is selected the HPV test will only be performed in the following scenarios:</p> <p>a. The pap test final diagnosis is NIL and the patient is between ages 30-64.</p> <p>b. The pap test final diagnosis is ASCUS and the patient is between ages 21-64.</p> <p>c. The pap test final diagnosis is LSIL and the patient is between ages 25-64 and is not pregnant.</p> <p>c. The HPV Genotype test will automatically reflex for all patients between the ages of 30-64 with a NIL pap test diagnosis and a positive HPV test diagnosis.</p> <p>1. Note: Add on HPV and HPV Genotype tests can be added up to 4 weeks from the collection date</p> |
| Thyroid FNA resulting in diagnosis of AUS (Atypia of undetermined significance) and SFN (Suspicious for follicular neoplasm); Indeterminate Bethesda categories (when no concurrent malignancy is present)<br><small style="display: block; text-align: right;">As per NCCN guidelines- added 2/2023</small> | Afirma Genomic Sequencing Classifier (GSC) and Malignancy Classifiers (BRAF, MTC, RET/PTC1 and RET/PTC3); Veracyte  |
| <b>Cytology– Optional</b>  |   |
| <b>Initial Test and Result</b>   | <b>Optional Follow up Testing</b>   |
| Cervical Cytology with ASCUS, ASC-H OR LSIL  | HPV-high risk   |
| Cervical Cytology with ASCUS or AGUS   | HPV   |
| Cervical Cytology with NIL, ASCUS or AGUS  | HPV   |



## Flow Cytometry Reflex Testing

| <b>Flow Cytometry – Mandatory</b>  |  |
|--|--|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>  |
| Diagnostic sample of B-lymphoblastic leukemia (B-ALL) and B-cell non-Hodgkin lymphoma with anti CD-19 therapy  | Flow cytometry Blinatumomab tube (anti-CD19 therapy tubes)   |
| Flow cytometry testing requiring CBC w diff for quantitation of flow cytometry results (i.e. SCID, ALPS, lymph subsets, CD20, etc)   | <ol style="list-style-type: none"> <li>1. CBC w diff on all orders that do not already have a CBC w diff ordered on patient on the same date and specimen is less than 10 hours old.</li> <li>2. And Flow cytometry is unable to get WBC and automated differential.</li> </ol>  |
| <p>Leukemia/Lymphoma/Myeloma and/or Non-Hodgkin lymphoma panels by flow cytometry: if indicated, reflex testing may be added to further characterize possible abnormal cell populations identified by the screening panel.</p> <p>These panels are reviewed continuously in multidisciplinary conferences and by the flow cytometry laboratory and hematopathologists.</p> | <p>The following add on panels may be employed after initial testing, as needed and appropriate, to further evaluate any possible abnormal population of cells.</p> <p>B lymphoblastic leukemia (B-ALL) panel<br/> T lymphoblastic leukemia (T-ALL) panel<br/> Chronic lymphocytic leukemia (CLL) panel<br/> Hairy cell leukemia (HCL) panel<br/> Extended B-cell tube panel<br/> Extended T-cell tube panel<br/> NK cell or LGL panel<br/> CD10 positive B-cell panel<br/> CD5 positive B-cell panel<br/> Acute myeloid leukemia (AML) panel<br/> Extended myeloid or monocytic panel<br/> Plasma cell panel<br/> Mast cell panel</p> |
| <b>Flow Cytometry – Optional</b>   |  |
| <b>Initial Test and Result</b>   | <b>Optional Follow up Testing</b>  |
| Fetal Cells by Flow Cytometry →<br>If ordered STAT and received in lab outside of flow cytometry testing hours (after 3:30 Mon-Fri or after 10:00am Sat or Sun)  | Fetal Hemoglobin by Kleihauer Betke performed in place of flow cytometry   |
| <p>Leukemia or Non-Hodgkin Lymphoma Panel by Flow Cytometry →</p> <p>Cell population is diagnostic of circulating leukemia/lymphoma/myeloma, and patients under age of 80 with new diagnosis</p>   | FISH testing   |

## Hematology Reflex Testing

| <b>Hematology – Mandatory</b>   |   |
|---|---|
| <b>Initial Test and Result</b>  | <b>Confirmation Testing/Additional Workup</b>   |
| CBC w/ diff - will reflex to CBC w/out diff "if" the WBC is less than <b>or equal to 0.4.</b><br><small>Updated by Lab due to OEE March 2024</small>  | CBC w/out differential  |
| Cerebral Spinal Fluid (CSF) RBC Cell Count greater than or equal to 400 cells in tube 3<br><small>Update Approved by MEC May 2022</small>   | Additional count of tube 1  |
| Cerebral Spinal Fluid (CSF) WBC Cell Count greater than 0, in tube 3  | Manual differential   |
| Mononucleosis Screen, Epstein Barr (EBV) IgM if Negative: If Mononucleosis Screen is Negative   | Epstein Barr (EBV) VCA IgM Acute Antibody   |
| Malaria Rapid Screen <ol style="list-style-type: none"> <li>1. If presumptive positive for malaria antigens</li> <li>2. If presumptive negative for malaria antigens</li> </ol>   | <ol style="list-style-type: none"> <li>1. Parasitemia Level; Malaria speciation confirmation by thin/thick smear microscopy evaluation</li> <li>2. Negative result confirmed by thin/thick smear microscopy evaluation. If smear is positive, then reflex to Parasitemia Level</li> </ol> |
| Pathologist Review<br>If review of peripheral blood smear is ordered without required accompanying CBC with differential, and if the specimen is within 10 hours of collection.   | Complete Blood Count (CBC) with Differential  |
| Platelet Count less than 100,000/ $\mu$ L<br><small>Updated November 2021</small>   | Immature platelet fraction (IPF)  |
| <b>Hematology – Optional</b>  |   |
| <b>Initial Test and Result</b>  | <b>Optional Follow up Testing</b>   |
| CBC order →   | Pathologist review  |
| CBC specimens that fulfill criteria listed in <a href="#">Pathologist Review</a>  |   |
| CBC w/ Diff →   | Pathologist Review  |
| CBC specimens that fulfill criteria listed in <a href="#">Pathologist Review</a>  |   |
| CBC w/ Diff →<br><br>WBC less than 3.0 or greater than 18.0<br>HGB less than 8.0 or greater than 18.0<br>MCV less than 75.0 or greater than 110.0 (updated 04/2021)<br>Absolute neut count less than 1.50 or greater than 9.00<br>Absolute lymph count less than 0.39 or greater than 4.50<br>Absolute mono count greater than 1.50<br>Absolute eos count greater than 1.00<br>Absolute bas count greater than 0.20<br>Abnormal instrument flags suggesting abnormality | Manual WBC differential   |
| Cell Ct only BFL order →<br>Body fluid specimens that fulfill criteria listed in <a href="#">Pathologist Review</a>   | Pathologist review  |

## Hematopathology Reflex Testing

| <b>Hematopathology – Mandatory</b>   |  |
|--|--|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>  |
| Acute myeloid leukemia <b>and myeloid neoplasms (includes MDS, MDS/MPN, and PMF—not CML, ET or P vera)</b> : new diagnosis, <b>patient of any age</b> (Bone Marrow or Whole Blood) | Heme Molecular Sequence Analysis   |
| All newly diagnosed patients with B-Cell Lymphomas with features concerning possible lymphoplasmacytic, unless otherwise specified by physician                                    | <ul style="list-style-type: none"> <li>• MYD88 L265P mutation testing on bone marrow aspirate</li> </ul>   |
| Diffuse large B-cell lymphoma: new diagnosis, <b>patient of any age</b>  | DLBCL panel by IHC (CD3, CD20, CD5, CD10, BCL-1, Ki-67, EBERish, BCL-2, BCL-6, MUM1, MYC, CD30, and CD45), FISH for high grade B-cell lymphoma (double hit BCL-2, BCL-6, MYC, with t(8;14) reflex) |
| New diagnosis of neoplastic hematopoietic population by leukemia/lymphoma/myeloma flow cytometry panel <b>patient of any age</b>   | FISH testing as appropriate (use especially for new diagnosis of CLL in peripheral blood)  |
| Bone marrow or blood EDTA samples (Philadelphia positive B-ALL and CML)  | RNA extract and hold   |

## Immunochemistry Reflex Testing

| <b>Immunochemistry – Mandatory</b>  |  |
|---|--|
| <b>Initial Test and Result</b>  | <b>Confirmation Testing/Additional Workup</b>  |
| IFA AntiNuclear Antibody (ANA) Hep-2 Substrate with Reflex positive   | AntiNuclear Antibody (ANA) Titer and Pattern   |
| Celiac Disease Cascade<br><br>Transglutaminase (TTG) IgA antibody and total IgA performed<br><br><span style="float: right;">Updated February 2024</span> | <ul style="list-style-type: none"> <li>• Normal total IgA, <b>weak positive</b> TTG IgA (15-30U/mL): reflex Endomysial IgA</li> <li>• Low total IgA, negative TTG IgA (<math>\leq 6.9</math>U/mL): reflex TTG IgG, Gliadin IgG, and Gliadin IgA</li> <li>• Low total IgA, positive TTG IgA (<math>\geq 10.1</math>U/mL): reflex TTG IgG, Gliadin IgG, and Gliadin IgA</li> <li>• Low total IgA, <b>weak positive</b> TTG IgA (15-30 U/mL): reflex TTG IgG, Gliadin IgG, Gliadin IgA, and Endomysial IgA</li> </ul> |
| Hemoglobin (Hgb) A2 result is greater than 10%  | Capillarys Hemoglobin Electrophoresis (to confirm Hgb E)   |
| Hemoglobin Fractionation that identifies new Hemoglobin S   | Sickle Cell Screen   |
| Hemoglobin Fractionation  | CBC on all orders for Hemoglobin Fractionation that do not already have a CBC ordered in the past 30 days.   |
| Patient is less than 6 months of age and has suspected Hgb S by the Hgb fractionation test  | Capillarys Hemoglobin Electrophoresis  |
| Patient is suspected of having Hgb C by the Hgb fractionation test  | Capillarys Hemoglobin Electrophoresis  |
| Positive Cryoglobulin test<br><br><span style="float: right;">Updated May 2024</span>   | Positive Cryoglobulins which have not had an identification in the past 12 months will have the Reflex Cryoglobulin Interpretation ordered.  |
| Positive Lyme Disease Screen  | Western Blot   |
| Rapid Plasma Reagin (RPR) test for syphilis   | SYPHILIS IgG SCREEN will be performed instead of the RPR.  |
| Random Urine Protein Electrophoresis IFE if indicated   | For order questions of Monitoring or General screen: reflex to urine immunofixation if abnormal protein electrophoresis. For order questions of AL amyloid: always reflex to urine immunofixation.   |
| Serum Protein Electrophoresis IFE if indicated  | For order questions of Monitoring or General screen: reflex to serum immunofixation if abnormal protein electrophoresis. For order questions of AL amyloid and neuropathy: always reflex to serum immunofixation.  |
| 24-hour Urine Protein Electrophoresis IFE if indicated  | For order questions of Monitoring or General screen: reflex to urine immunofixation if abnormal protein electrophoresis. For order questions of AL amyloid: always reflex to urine immunofixation.   |
| <b>Immunochemistry – Optional</b>   |  |
| <b>Initial Test and Result</b>  | <b>Optional Follow Up Testing</b>  |
| ANA screen order →  | ANA Hep2 (IFA) if positive reflex to titer. If titer is equal or greater than 1:160 reflex to Anti-dsDNA,  |

|   |  |
|---|--|
| If positive ANA   | anti-Sm, anti-RNP, anti-SSA, anti-SSB, anti Scl70, anti-centromere and anti-Jo1  |
| Peanut IgE reflex order →<br>Peanut IgE => 0.35 kU/L<br>Updated February 2024 | Peanut component allergen panel (Peanut Ara h 1 IgE, Peanut Ara h 2 IgE, Peanut Ara h 3 IgE, Peanut Ara h 6 IgE, Peanut Ara h 8 IgE, and Peanut Ara h 9 IgE) |
| Egg IgE reflex order →<br>Egg white IgE => 0.35 kU/L<br>Updated February 2024 | Egg component allergen Panel (Ovomucoid IgE and Ovalbumin IgE)   |
| Milk IgE reflex order →<br>Milk (cow) => 0.35 kU/L<br>Updated February 2024   | Milk component allergen Panel (Casein IgE, Alpha-Lactalbumin IgE, and Beta-lactoglobulin IgE)  |

## Microbiology Reflex Testing

| <b>Microbiology – Mandatory</b>  |  |
|--|--|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>  |
| Anaerobic Culture  | Aerobic culture on all orders that do not already have an aerobic culture ordered on the same specimen.  |
| Blood Culture; if positive for growth of bacteria or yeast   | <ul style="list-style-type: none"> <li>• Organism identification will be performed if growth occurs any bottle.</li> <li>• Antimicrobial susceptibility testing will be performed depending on organism identification as per protocol.</li> </ul> |
| Body Fluid culture greater than 1mL sample with only aerobic culture   | Add anaerobic culture  |
| Cryptococcus Antigen ordered on CSF  | Fungal Culture order is added in addition to Cryptococcus Ag testing.  |
| Clostridioides difficile by PCR  | Clostridioides difficile PCR testing may only be ordered with approval from Infectious Disease. Other PCR orders are switched to C. difficile toxin EIA.   |
| Culture from catheter tip or foreign bodies  | Foreign body culture   |
| Group A Streptococcus negative antigen test on pediatric patients  | Add throat Culture   |
| Positive culture for pathogen or organism with clinically significant concentration (bacteria or yeast)                        | Susceptibility and typing as necessary.  |
| Positive Group B Strep, Penicillin allergy, PCR  | Susceptibility testing.  |
| Tissue Specimens ordered as a Body Fluid Culture   | Cancel and Order as a Tissue Culture   |
| Body Fluid Specimens ordered as a Tissue Culture   | Cancel and Order as a Body Fluid Culture   |
| HSV viral culture from cutaneous and mucocutaneous lesions   | Cancel and change to HSV PCR order   |
| Viral Cultures from swab specimens <ol style="list-style-type: none"> <li>1. Dermal Swabs</li> <li>2. Genital Swabs</li> </ol> | PCR <ol style="list-style-type: none"> <li>1. Dermal Swab - HSV PCR and VZV PCR</li> <li>2. Genital Swab - HSV PCR</li> </ol>  |

Approved by MEC March 2022

## Molecular Diagnostics Reflex Testing

| <b>Molecular Diagnostics – Mandatory</b>   |   |
|--|---|
| <b>Initial Test and Result</b>   | <b>Confirmation Testing/Additional Workup</b>   |
| Myeloproliferative Neoplasms (MPN)<br>1. JAK2 V617F ordered without prior 12-month BCR-ABL<br>2. JAK2 V617F mutation negative with BCR-ABL negative within past 12 months. | 1. BCR-ABL must be performed first if Negative then JAK2 V617F performed<br>2. 2.Then MPN Expanded Panel  |
| Specimens in Abbott Multi Collect tube ordered as Aptima specimens.<br><br><div style="text-align: right;">Updated March 2024</div>  | Cancel Aptima test and reorder corresponding Abbott test for Chlamydia PCR, Gonococcus PCR, Trichomonas PCR, Mycoplasma Genitalium PCR, STI Panel (Alinity)     |
| Specimens in Aptima collection tube ordered as Abbott Multi Collect tube specimens.<br><br><div style="text-align: right;">Updated March 2024</div>                        | Cancel Abbott test and reorder corresponding Aptima test for Chlamydia NAAT, Gonococcus NAAT, or Trichomonas NAAT, Mycoplasma Genitalium NAAT, Aptima STI Panel |
| Female urine specimens with Trichomonas Antigen testing ordered.<br><br><div style="text-align: right;">November 2022</div>  | Cancel Trichomonas Antigen order and reorder as corresponding Trichomonas PCR order.  |
| Specimens in Thinprep vial ordered as Abbott Multi Collect tube specimen.<br><br><div style="text-align: right;">March 2024</div>  | Cancel Abbott test and reorder corresponding Aptima test for Chlamydia NAAT, Gonococcus NAAT, or Trichomonas NAAT, Mycoplasma Genitalium NAAT, Aptima STI Panel |
| Male urine specimen collected in Abbott Multi Collect tube or Aptima tube and ordered as Trichomonas Antigen<br><br><div style="text-align: right;">March 2024</div>       | Cancel Trichomonas Antigen order and reorder as corresponding Trichomonas PCR order.  |

## Referrals Reflex Testing

| <b>Referrals – Mandatory</b>                             |   |
|--|---|
| <b>Initial Test and Result</b>                           | <b>Confirmation Testing/Additional Workup</b> |
| Positive Gamma HydroxyButyrate (GHB)                     | GC/MS Confirmation (Mayo)                     |
| Blastomyces Antibody by EIA, Serum equivocal or Positive | Blastomyces Antibody by Immunodiffusion       |



## Toxicology Reflex Testing

| Toxicology – Mandatory  |   |
|---|---|
| Initial Test and Result   | Confirmation Testing/Additional Workup                              |
| For obstetric inpatients (Mothers and their babies): Positive Amphetamine, Cannabinoids, Ethanol, Methadone, opiates, Oxycodone or cocaine on a Drug of Abuse screen.<br>For OB 330 Residency: any positive analytes on a Drug of Abuse screen. | LC/MS Confirmation  |
| Positive opiates on Comprehensive Drug Screens  | LC/MS Confirmation  |
| Lead Screen, Filter Paper order with whole blood sample.<br><br><div style="text-align: right;">June 2023</div>   | Change order to Lead, Blood Level to match provided sample.         |
| Lead, Blood Level order with filter paper sample collected.<br><br><div style="text-align: right;">June 2023</div>  | Change order to Lead Screen, Filter Paper to match provided sample. |

## Transfusion Medicine/Blood Bank Reflex Testing

| <b>Transfusion Medicine – Mandatory</b>   |   |
|---|---|
| <b>Initial Test and Result</b>  | <b>Confirmation Testing/Additional Workup</b>   |
| Antibody Screens  | ABO/RH  |
| Antibody Titer  | ABO/Rh and Antibody Screen  |
| All patients that are identified with hemoglobinopathy including: <ul style="list-style-type: none"> <li>• hgSS</li> <li>• hgSC</li> <li>• beta thalassemia</li> </ul> And have not been transfused in the last 3 months. | Serological C, E, and K antigen typing  |
| NICU patients with a cord blood workup  | Antibody Screen   |
| Positive Antibody Screen, or a positive Direct Antiglobulin Test (DAT) on inpatients, outpatients, and surgical patients  | Relevant studies as needed including antibody identification, antigen typing, direct antiglobulin test, elution and absorption. In addition, packed blood cells will be antigen typed and crossmatched.                           |
| Positive prenatal Profile Type & Antibody Screen  | Antibody identification with titer if identified antibody is clinically significant   |
| Women of childbearing age identified as RHD variants or "weak D phenotypes" via serological testing with no previous RHD genotyping on file.  | Molecular RHD Genotyping  |
| Type & Screen (T&S) on a patient with autologous or directed units  | Crossmatch of the units   |
| Type & Screen (T&S) on a pre-op patient with an antibody  | Crossmatch of two antigen negative units  |
| Patients with difficult antibody situation (e.g., red cell autoantibodies, multiple red cell antibodies or atypical serologic difficulties due to medication, rare antisera or broad serologic reactivity)                | Testing for red cell genotyping (molecular testing) to further determine patient management, as deemed necessary by the Blood Bank physician/pathologist.<br><small>For more details, please see original MEC from 8/2021</small> |
| <b>Known Sickle cell disease or thalassemia patient that is requiring transfusion and has not had a prior Red Cell Genotyping Panel</b><br><span style="float: right;"><b>May 2024</b></span>                             | <b>Red Cell Genotyping Panel. Lab Referrals Misc 848</b>  |

## Urinalysis Reflex Testing

| <b>Urinalysis – Mandatory</b>   |   |
|---|---|
| <b>Initial Test and Result</b>  | <b>Confirmation Testing/Additional Workup</b> |
| UA or UA culture if with inadequate volume for microscopic exam   | Urine Dipstick (U dip)                        |
| <b>Urinalysis – Optional</b>  |   |
| <b>Initial Test and Result</b>  | <b>Optional Follow Up Testing</b>             |
| If urinalysis (UA) with two or more of the following abnormal findings, provided there are less than 10 squamous epithelial cells observed per high power field:<br>-Greater than or equal to 10 WBC<br>-Positive leukocyte esterase<br>-Positive nitrite<br>OR if specimen is<br>-Grossly bloody | Urine Culture                                 |
| If volume is inadequate for microscopic exam and Urine Dipstick (U dip) with one or more of the following abnormal findings:<br>-Positive leukocyte esterase<br>-Positive nitrite   | Urine Culture                                 |