#### **REFLEX TESTING**

Administrative Procedure # 822.A

Reflex testing is a necessary follow-up for the testing listed below. This testing is required to confirm quantitative positive preliminary testing and/or specified screening tests, or to provide Pathology Physician review and interpretation with written report.

| Test   | Condition(s)                            | Reflex Test(s)  |
|--|---|---|
| IMMUNOLOGY & FL  | OW CYTOMETRY                            |   |
| Anti-Mitochondrial<br>Antibody (AMA)                   | Positive                                | AMA Titer   |
| Anti-Smooth<br>Muscle Antibody<br>(ASMA)               | Positive                                | ASMA Titer  |
| Anti-Parietal Cell<br>Antibody (APCA)                  | Positive                                | APCA Titer  |
| Protein<br>Electrophoresis<br>(PEP)                    | Suspicious Pattern                      | Immunofixation Electrophoresis (IFE)  |
| Flow Cytometry   | All                                     | Pathologist Interpretation  |
| Protein<br>Electrophoresis<br>(PEP)                    | All                                     | Pathologist Interpretation  |
| Immunofixation<br>Electrophoresis<br>(IFE)             | All                                     | Pathologist Interpretation  |
| HEMATOLOGY & HE  | EMOSTASIS                               |   |
| Hemoglobin Screen                                      | Abnormal                                | Gel Electrophoresis and/or KB,<br>Solubility, Peripheral Blood Smear,<br>Send out for Hemoglobin Analysis<br>confirmation using an alternative method<br>per SOP. |
| Gel Electrophoresis                                    | Abnormal                                | KB and/or Solubility, Peripheral Blood<br>Smear, Send out for Hemoglobin Analysis<br>confirmation using an alternate method<br>per SOP                            |
| Hemoglobin<br>Analysis, No<br>Interpretation           | First time abnormal hemoglobin analysis | Pathologist Interpretation  |
| Rapid Malaria<br>Screen                                | Positive                                | Blood parasite screen   |
| ADAMTS-13<br>activity                                  | <30%                                    | ADAMTS-13 inhibitor assay/titer   |
| ADAMTS-13<br>inhibitor                                 | < 0.7 Inhibitor Units                   | ADAMTS-13 Antibody  |
| Coagulation profile studies                            | Bleeding or thrombophilia<br>work-ups   | Pathologist Interpretation  |
| Dilute Russell's<br>Viper Venom Time<br>(DRVVT) Screen | Prolonged                               | DRVVT Confirmation test   |
| Thrombin Time  | Prolonged                               | Protamine Correction or Plasma Mixing<br>Test   |

# **REFLEX TESTING**

| Test   | Condition(s)  |   | Reflex Test(s)   |
|--|---|---|--|
| Von Willebrand   | Per Pathologist discretion based on results and clinical              |   | VWF multimer   |
| Disease Testing  |   | history.  |  |
| CBC with Diff  |   | Abnormal  | Manual Differential  |
|  | Synovial Fluid  | All   | Pathologist Interpretation   |
| Fluid Studies  | CSF   | Previous or current diagnosis of<br>leukemia/lymphoma<br>or suspicious cell(s) in differential  | Pathologist Interpretation   |
|  | Body Fluid  | Suspicious cell(s) in differential  | Pathologist Interpretation   |
| Fluid Studies  | First time mali   | gnant, blasts or "other" cells seen   | Cytology   |
| Peripheral Blood<br>Smear                                      | Abnormal  |   | Pathologist Interpretation   |
| Heparin Induced<br>Thrombocytopenia<br>(HIT)                   | Positive  |   | Serotonin Release Assay (SRA)- Send<br>Out   |
| TRANSFUSION SE   | RVICES  |   |  |
| Antibody Screen  | Positive  |   | Antibody Identification (ID), Red Cell<br>Antigen phenotype, Direct Coombs<br>(DAT), Select Cell Antibody Screen,<br>Titer (OB patient), Pathologist Review;<br>Send out ABID; Weak D analysis; Partial<br>D analysis, Genotyping, Elution |
| Blood Type<br>(ABO/Rh)   | Blood Type Discrepancy  |   | Al lectin, DAT, Antibody Screen, Red<br>Cell Antigen Typing<br>(phenotype/genotype); Weak D analysis,<br>Partial D analysis, Pathologist Review  |
| Fetal Bleed Screen   |   | Positive  | Kleihauer-Betke, Pathologist Review  |
| Direct Coombs<br>(DAT)<br>Comprehensive                        | Positive  |   | Antibody Screen, Elution, Antibody ID;<br>Red Cell Antigen Genotyping, Pathologist<br>Review   |
| Cord Blood Test  | Incompatibility between Mom & Baby (ABO and/or<br>Non- ABO)           |   | MAIS, Antibody Screen, Antibody ID,<br>Red Cell Antigen phenotype, Pathologist<br>Review   |
| Transfusion<br>Reaction Panel (TR<br>Post)                     | Suspe   | cted transfusion reaction   | Pathologist Review; DAT comprehensive,<br>Transfusion RXN LG/SML VOL, GS   |
| AB ID (Antibody<br>Identification)                             | Antibody dete   | ected and/or difficult crossmatch   | Pathologist Review, Patient Antigen phenotyping  |
| Miscellaneous<br>Blood Bank<br>Processes                       | expiration date; tu<br>use of outdated bl<br>blood pro<br>withdrawal/ | lude use of rare antisera beyond<br>ransfusion of Rh incompatible units;<br>ood, Evaluation of special testing or<br>oduct requirements, Market<br>Lookback from blood supplier | Pathologist Review antigen phenotyping,<br>QA review for Market withdrawal   |
| Serologic<br>Crossmatch  | -   | rossmatch or auto control positive  | Pathologist Review; DAT; Send Out<br>ABID  |
| Blood Type (Bone<br>Marrow & HPC<br>Allogeneic<br>Transplants) |   | tibility between donor and recipient.<br>nown alloantibodies  | ABO and/or Alloantibody Titer(s)/<br>Isoagglutinin titers, Pathologist Review,<br>antigen phenotyping  |
| Blood Type (Rh)  |   | Weak D  | Weak D analysis; Partial D analysis,<br>Pathologist Review   |

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| Test  | Condition(s)  | Reflex Test(s)   |
|---|---|--|
| CHEMICTRY                                       |   |  |
| CHEMISTRY                                       |   |  |
| Hepatitis B Surface<br>Antigen                  | Reactive  | Neutralization Test  |
| Hepatitis B Core<br>Antibody, Total,<br>Reflex  | Reactive  | Hepatitis B Core Antibody, IgM   |
|   | Color other than "none" or "yellow", clarity other<br>than "clear", trace or greater for leukocyte esterase,<br>blood, protein, or positive for nitrite |  |
| Urinalysis-Complete                             |   | Microscopic Analysis<br>HIV Confirmation   |
| HIV<br>Antibody/Antigen<br>Combo Test           | Reactive  | HIV Confirmation   |
| ED Preg Syphilis<br>Scrn                        | Reactive  | Syphilis IgG/IgM Ab with Reflex  |
| Syphilis IgG/IgM<br>Ab with Reflex              | Reactive  | Confirmation by RPR and/or TPPA  |
| Amphetamine<br>Screen, Urine                    | Positive except ED patient  | Amphetamine/ Methamphetamine<br>Confirmation   |
| Acid/Neutral &<br>Basic Blood Drug<br>Screen GC | Positive  | Confirmation by Gas Chromatography<br>and/or Mass Spectrometry                               |
| Toxicology Basic                                | Positive  | Confirmation by Gas Chromatography   |
| Urine Drug Screen                               |   | and/or Mass Spectrometry   |
| Comprehensive<br>Urine Drug Screen              | Positive  | Confirmation by Gas Chromatography<br>and/or Mass Spectrometry                               |
| Anti-DNA Ab, IgG<br>w/reflex to IFA titer       | Positive  | DsDNA (Crithidia luciliae) Ab IgG by<br>IFA  |
| CYTOLOGY  |   |  |
| Cytology Gyn<br>(PAP) Cervical                  | Age >=25 & is Atypical Squamous Cells of<br>Undetermined Significance (ASCUS)   | High Risk HPV DNA (UCDH)   |
| Cytology Gyn<br>(PAP) Vaginal                   | Age >=25 & is Atypical Squamous Cells of<br>Undetermined Significance (ASCUS)   | High Risk HPV 16/18 PCR (Sendout)  |
| MICROBIOLOGY                                    |   |  |
| Ova & Larva<br>Helminth Test                    | Potential parasite seen, non-helminth ova or larva.   | Parasite Stain for identification or send<br>specimen to reference lab for<br>identification |
| GI (Gastrointestinal)<br>Panel                  | Positive- Bacterial pathogen  | Stool Culture and susceptibility testing when appropriate per protocol                       |
| GI (Gastrointestinal)                           |   | C. difficile Diagnostic Test when  |
| Panel   | Positive C. diff target   | appropriate per protocol<br>Susceptibility testing performed per                             |
| Group B Strep PCR                               | Detected in patient with penicillin allergy   | protocol   |
| Cryptococcal<br>Antigen, CSF<br>Source          | Initial Positive  | Culture Bacterial (includes gram stain)<br>and Culture Fungal.                               |
| Cryptococcal<br>Antigen                         | Positive  | Cryptococcal Antigen Titer   |

# **REFLEX TESTING**

| Test                                 | Condition(s)  | Reflex Test(s)  |
|--------------------------------------|---|---|
| Culture,<br>Bacti/Fungal/AFB         | Potential pathogen as detailed in protocols by specimen source  | Pathogen identification and/or<br>susceptibility testing  |
| Culture,<br>Bacti/Fungal/AFB         | Growth of organism demonstrating unusual or concerning antimicrobial resistance   | Test by alternate susceptibility or PCR<br>method in house or send isolate to<br>reference lab for confirmation               |
| Culture,<br>Bacti/Fungal/AFB         | Growth of organism not identified by routine<br>laboratory methods  | Test by alternate method in house or send isolate to reference lab for identification   |
| Culture, Bacti                       | Specimen is lower respiratory, body fluid, tissue,<br>wound, or other miscellaneous source  | Gram Stain  |
| Culture, Bacti                       | Specimen is Bronchial Brushing, Transtracheal/<br>Percutaneous Lung Aspirate, Lung Biopsy Tissue,<br>Bronchial Alveolar Lavage(BAL), or swab from any<br>of the above sources | Culture, Legionella   |
| Culture, Blood                       | Growth of bacteria or yeast   | Blood Culture ID by PCR and/or<br>susceptibility testing when appropriate per<br>protocol                                     |
| Culture/Smear, AFB                   | Smear positive for AFB  | MTb Nucleic Acid Amplification Test<br>performed on all first-time smear positive<br>patients OR 6 months from previous assay |
| MTB, PCR                             | All   | AFB Smear and Culture   |
| MOLECULAR<br>PATHOLOGY               |   |   |
| Cystic Fibrosis<br>mutation analysis | All   | Pathologist Interpretation  |
| Hereditary<br>Hemochromatosis        | All   | Pathologist Interpretation  |
| HER2 FISH                            | All   | Pathologist Interpretation  |
| CLL FISH                             | All   | Pathologist Interpretation  |
| HPV DNA Primary<br>Screening         | HPV (16,18, and/or High-Risk Group) positives   | Cytology Gyn (PAP test)   |
| SURGICAL<br>PATHOLOGY                |   |   |
| Surgical Pathology                   | Any Solid Tumor Malignancy  | HER2 IHC  |
| Cases                                | New diagnosis of primary or metastatic breast cancer<br>Diagnosis of breast cancer after neoadjuvant<br>chemotherapy  | ER, PR, AR, Ki67 and HER2/neu by<br>IHC; Her2 FISH for invasive cancers   |
|                                      | New Diagnosis of colon cancer   | DNA Mismatch repair testing by IHC<br>(MLH1, MSH2, MSH6, PMS2); testing<br>for BRAF if MLH1 and/or PMS2 is<br>abnormal.       |
|                                      | Small bowel carcinoma   | MMR IHC   |
|                                      | Squamous Cell Carcinoma of Oropharynx, Head, and neck (primary, recurrent, and metastatic).   | P16, HER2 IHC, PD-L1 IHC  |
|                                      | Squamous Cell Carcinoma or Dysplasia of Anogenital<br>Region (including cervix, vulva, anus, penis)   | P16   |

# **REFLEX TESTING**

| Test | Condition(s)   | Reflex Test(s)  |
|------|--|---|
|      | Heart Biopsy- Transplant                                     | Trichrome (HISTO), CD68 (IHC), and C4D (IF)   |
|      | New diagnosis of primary or metastatic lung cancer           | PD-L1 (IHC)   |
|      | Kidney-Biopsy Native   | PAS, Jones, Trichrome (HISTO)   |
|      |  | IgG, IgA, IgM, C3, C1q, kappa, lambda, fibrinogen, albumin, and FS-H&E  |
|      |  | Electron Microscopy (Send-Out)  |
|      | Kidneys-Biopsy Transplant                                    | PAS and Trichrome (HISTO)   |
|      |  | IgG, IgA, IgM, C3, C1q, fibrinogen,<br>albumin, FS-H&E, C4d (IF), and SV40  |
|      | Muscle Biopsies  | FS-Trichrome, FS-PAS, FS-H&E, Oil<br>Red O, NADH, ATPase pH 4.3, ATPase<br>pH 9.4, COX/SDH (combined stain),<br>Acid Phosphatase, NSE(non-specific<br>esterase), Myophosphorylase, Alkaline<br>phosphatase, SDH, ATPase pH4.6 |
|      | Nerve Biopsies   | Toluidine blue stain of glutaraldehyde<br>fixed tissue on thick section (Send-Out)  |
|      | Neuroblastoma  | N-MYC FISH (Send-Out)   |
|      | All Gliomas  | IDH1, ATRX, p53, Ki67   |
|      | All pituitary adenomas                                       | Ki67, cam5.2 (In house)<br>Pit1, TPit, SF1, GH, Prolactin, TSH,<br>ACTH (Send-Out)  |
|      | Ependymomas of Posterior Fossa                               | H3K27me3 (IHC Send-Out)   |
|      | All Meningiomas  | Ki67  |
|      | Liver Biopsy   | Reticulin, Trichrome, Iron, PAS and<br>PASD Stains. (HISTO)   |
|      | New diagnosis of endometrial cancer                          | DNA Mismatch repair testing by IHC<br>(MLH1, MSH2, MSH6, PMS2); testing<br>for promoter methylation if MLH1 and/or<br>PMS2 is abnormal, p53 (IHC)   |
|      | Sentinel lymph nodes, Melanoma of skin                       | Melan-A (IHC) or HMB-45 (IHC) or<br>SOX10 (IHC) each block  |
|      | Sentinel lymph nodes, gynecologic tract cancer               | Pancytokeratins (IHC, x2; ultrastaging)   |
|      | Endometrial Carcinoma  | For Non-Serous Carcinoma: p53 and<br>MMR (IHC). POLE Sequencing<br>(Stanford Send-Out)  |
|      |  | For Serous Carcinoma: HER2/neu (IHC and FISH)   |
|      | New Diagnosis of primary or metastatic melanoma (any tissue) | BRAF-V600E  |
|      | Carcinoma of the ovary                                       | P53 and Mismatch repair analysis by IHC<br>for all endometrioid and clear cell<br>carcinomas POLE Sequencing (Stanford<br>Send-Out), HER2 IHC   |
|      | Vulvar Carcinoma   | P16 and p53 (IHC)   |

# **REFLEX TESTING**

# Administrative Procedure # 822.A

| Test  | Condition(s)   | Reflex Test(s)  |
|---|--|---|
|   | Mucinous neoplasm of ovary                                 | P53 or HER2 (IHC and FISH)  |
|   | Tenosynovial biopsy, Positive Congo red stain for amyloid. | Send-out to Mayo Clinic for subtyping by<br>mass spectrometry                                 |
|   | Non-small cell carcinoma of lung.                          | HER2 IHC  |
|   | Bone Marrow  | Bone Marrow Clot Section: Iron,<br>Reticulin<br>Bone Marrow Core Biopsy: PAS and<br>Reticulin |
|   | Fingernail and Toenail                                     | Alcian Blue-PAS   |
|   | Temporal Artery, Biopsy                                    | Elastic-EVG   |
| MGMT promoter<br>methylation (Send-<br>Out)   | All  | Pathologist Interpretation  |
| TERT Mutation<br>(Send-Out)                   | All  | Pathologist Interpretation  |
| IDH1/IDH2<br>Mutation Analysis<br>(Send-Out)  | All  | Pathologist Interpretation  |
| CDKN2A FISH<br>(Send-Out)                     | All  | Pathologist Interpretation  |
| BRAF V600E<br>Mutation Analysis<br>(Send-Out) | All  | Pathologist Interpretation  |
| H3K27M Mutation<br>(IHC) (Send-Out)           | All  | Pathologist Interpretation  |
| H3K27me3 (IHC)<br>(Send-Out)                  | All  | Pathologist Interpretation  |
| H3G34 R/V (IHC)<br>(Send-Out)                 | All  | Pathologist Interpretation  |
| EWSR FISH (Send-<br>Out)                      | All  | Pathologist Interpretation  |
| DDIT3 FISH (Send-<br>Out)                     | All  | Pathologist Interpretation  |
| SYT FISH (Send-<br>Out)                       | All  | Pathologist Interpretation  |
| USP6 FISH (Send-<br>Out)                      | All  | Pathologist Interpretation  |
| POLE Sequencing<br>(Stanford Send-Out)        | All  | Pathologist Interpretation  |

This list of reflex testing has been reviewed and approved by the UCDMC Medical Staff

#### **REFLEX TESTING**

Administrative Procedure # 822.A

Executive Committee.

DocuSigned by: 2l 13FA9A84ACC94A

7/17/2025

Clara K Paik, MD Chair, Medical Staff Executive Committee (Interim)

Date