700 Spring Garden Street
Philadelphia, PA 19123
(215) 451-4917
(215) 451-2506

Testing Performed by the

AABB Molecular Accredited

American Red Cross

National Molecular Laboratory

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National Molecular Laboratory

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Philadelphia, PA 19123

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Hours: M-F 7:00 am – 6:30 pm

Director: Dr Martin CH Chou, PhD

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CLIA License: 39D0194473

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Starting Material and Shipping Requirements for National Molecular Laboratory

All samples must be clearly labeled with the full name of the individual and a unique identification number. The information on the tube must match the information on the service request form. Requests should include date of collection.

Whole Blood should be collected in 5-10 ml EDTA (lavender top) tubes. Samples less than 10 days old are preferred. DNA yield from older specimens may be low or QNS. Whole blood specimens submitted for cDNA analysis should be collected with more than 90 days since transfusion of red cell products.

Whole blood sample can be shipped at room temperature or refrigerated using ice packs or wet ice sealed in plastic bags, according to DOT regulations for biological specimens.

Buccal swabs may be acceptable depending on the testing requested; contact the laboratory for more information. Buccal swabs should use a cotton-tipped applicator and be air dried completely before putting in a clean tube and shipping on ice packs or wet ice sealed in plastic bags.

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Human Erythrocyte Antigen (HEA) Genotyping Panel
Test Code SREF-IVD
Recommended CPT Code 0001U x 1

An FDA-cleared multi-analyte test performed on DNA from whole blood provides a predicted phenotype for 36 antigens.

Panel incudes C, c, E, e, V, VS, K, k, Kp^a, Kp^b, Js^a, Js^b, Fy^a, Fy^b, Fy^x, FY GATA, Jk^a, Jk^b, M, N, S, s, U, U^{VAR}, Lu^a, Lu^b, Di^a, Di^b, Co^a, Co^b, Do^a, Do^b, Hy, Jo^a, LW^a, LW^b, Sc1, Sc2 and HgbS.

This testing is useful when antigen status cannot be determined serologically, either because of recent transfusion, positive direct antiglobulin test or when serologic reagents are not available. The HEA genotyping panel is useful in patients being treated with immunotherapies including anti-CD38 and anti-CD47. The extended antigen phenotype prediction is also useful in patients on chronic transfusion regimens such as those with sickle cell disease and thalassemia. In alloimmunized patients, it can be used to assess the additional alloimmunization risk.

RHD Genotyping for D variants
Most Common Test Code: SREF-RHD
Recommended CPT Code: 81403 x 1

Additional test codes (and CPT codes):
SREF200B (81400), SREF250D (81401), SREFSEQD (81403), SREF500D (81403), SREF550D (81403), SREF750D (81403)

RHD Genotyping is used to identify *RHD* variant alleles and predict the D antigen phenotype. There are many *RHD* variant alleles and variants can have altered antigen expression and/or altered epitopes. *RHD* variants are found in all ethnic groups but are most common in individuals of African descent. Weak or altered antigen expression can lead to a serologic weak D phenotype. This is especially important in pregnant women and women of child-bearing age, as the decision regarding RhIg prophylaxis is informed by *RHD* variant type. Specifically, individuals who are weak D types 1, 2 and 3 are not at risk of D alloimmunization. Weak or altered RhD antigen expression can also result in a typing discrepancy, either between test methods, reagents, laboratories or between a current and historic type. *RHD* genotyping is performed using a commercially available “Research Use Only” genotyping panel that can detect many weak, Del and partial alleles including weak D types 1, 2 and 3 along with detection of variants associated with low-prevalence antigens such as Go(a) and DAK. One or more lab-developed tests may be performed to rule out weak or partial alleles not interrogated on the commercial panel. High-resolution Sanger sequencing of genomic DNA is used to rule out rare or novel alleles. High-resolution Sanger sequencing of cDNA analysis can be used to characterize transcripts and resolve equivocal allele status of compound heterozygous samples or suspected splice site variants. All RH testing is “Research Use Only”.

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RHCE Genotyping for C, c, E and e variants including hr^B and hr^S status

Most Common Test Code: SREF450
Recommended CPT Code: 81403 x 1

Additional test codes (and CPT codes):
SREF200C (81400), SREF250H (81401), SREFSEQD (81403), SREF500C (81403), SREF550C (81403), SREF750C (81403)

RHCE Genotyping is used to identify *RHCE* variant alleles and can predict C, c, E, e antigen phenotypes. In addition, this testing can detect many *RHCE* variant alleles that are associated with weakened or altered antigen expression, loss of high-prevalence antigens (e.g. hr^B, hr^S) or gain of low-prevalence antigens (e.g., V, VS). *RHCE* variants are found in all ethnic groups but are most common in individuals of African descent. Weak antigen expression can lead to typing discrepancies, for example with e and C antigens. Patients who express altered antigens can be at risk of alloimmunization (eg., e+ with anti-e or C+ with anti-C). *RHCE* genotyping is performed using a commercially-available "Research Use Only" genotyping panel that can detect many common altered alleles along with detection of variants associated with low-prevalence antigens such as V and VS as well as C^w, C^x and JAL. One or more lab-developed tests may be performed to rule out variant alleles not interrogated on the commercial panel. High-resolution sequence-based typing (SBT) is used to rule out rare or novel alleles. High-resolution Sanger sequencing of cDNA can be used to characterize transcripts and resolve equivocal allele status of compound heterozygous samples or suspected splice site variants. All RH testing is "Research Use Only".

RH Characterization
Test Codes SREF-RHD and SREF450
Additional Tests may include SREF750, SREF-SEQ, SREF500, SREF550
Recommended CPT Code 81403 x each

RHD variant and *RHCE* variant alleles are often co-inherited and are not uncommon in individuals of African descent. Patients who are found to have D variants may be at risk of expressing altered *RHCE* antigens and visa-versa. Patients of African descent who are likely to be multiply or chronically transfused may benefit from *RH* characterization. *RH* characterization includes use of *RHD* and *RHCE* commercially-available "Research Use Only" genotyping panels and may also include performance of one or more lab-developed tests to rule out variant alleles not interrogated on these commercial panels. High-resolution sequence-based typing (SBT) is used to rule out rare or novel alleles. High-resolution Sanger sequencing of cDNA can be used to characterize transcripts and resolve equivocal allele status of compound heterozygous samples or suspected splice site variants. All RH testing is "Research Use Only".

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RHD Zygosity
Test codes include SREF200B, SREF200D, SREF250B, SREF250H
Recommended CPT codes: 81400x2, 81401x2

It is not uncommon to be hemizygous for *RHD* alleles. The *RHD* zygosity status of a D+ partner of an RhD negative woman with anti-D can be used to determine if the partner carries one or two *RHD* alleles and determine chance that an offspring of the couple would express the RhD antigen. *RHD* zygosity includes several "Research Use Only" lab-developed tests.

ABO Genotyping, Medium Resolution
Test Code SREFABRT
Recommended CPT Code 81403 x 1

Determination of ABO common alleles (*ABO*A, ABO*B, ABO*O1, ABO*O2*) and some variant alleles encoding subgroups (ex. *ABO**A2, *ABO**A3) can be helpful in investigating discrepancies between forward and reverse type or current and historic serologic testing. This testing cannot rule out the presence of all subgroups. This testing uses a commercially-available "Research Use Only" genotyping panel.

ABO Genotyping, High Resolution
Test Code SREF550A
Recommended CPT Code 81403 x 1

When medium-resolution ABO genotyping does not resolve an ABO discrepancy or unexpected serologic result, high resolution ABO genotyping may be warranted. Uncommon and rare ABO variant alleles (eg., *ABO*B(A), ABO*cisAB, ABO*Ax, ABO*Aw*) can be identified using "Research Use Only" sequence-based typing (SBT).

Non Rh, Non ABO Variants
Test Codes include SREFSEQ series, SREF500 series, SREF750 series (call for specific codes)
Recommended CPT Code 81403 x each

Typing discrepancies or suspected alloantibodies to non-Rh blood group systems may benefit from molecular testing. Blood group systems include MNS, LU, KEL, FY, JK, DO, KN, YT, and XK. The *KLF1* gene can be interrogated to rule out a possible *In(Lu)* phenotype. For example, a patient who is Jk(a+) with allo-Jk^{a} may express a Jk^{a} variant that is associated with alloimmunization. In addition, variant testing can be useful in resolving discrepancies between serologic testing and the phenotype predicted by the HEA genotyping panel (described above).

This testing is performed using lab-developed tests using gel-based genotyping including sequence-specific primer PCR (SSP-PCR) and sequence-based typing (SBT). High-resolution Sanger sequencing of cDNA can be used to resolve equivocal allele status of compound heterozygous samples or suspected splice site variants in RH, MNS, JK, KEL and LU systems.

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Human Platelet Antigen (HPA) Genotyping Panel
Test Codes SR81400A, SREFHPA2, SREFHPA3, SREFHPA4, SREFHPA5, SREFHPA6, SREFHPA9, SREFHP15
Recommended CPT Codes 81105-81112, x 1 each

A single multi-analyte test performed on genomic DNA provides a predicted phenotype for antigens HPA-1a/1b, HPA-2a/2b, HPA-3a/3b, HPA-4a/4b, HPA-5a/5b, HPA-6a/6b, HPA-9a/9b and HPA-15a/15b. This testing is useful when antigen status cannot be determined serologically. The extended antigen phenotype prediction is useful in workups of suspected Fetal/Neonatal Alloimmune Thrombocytopenia (FNAIT). In platelet refractory patients in whom HLA antibodies have been ruled out, it can be used to assess alloimmunization and select platelet products.