The Red Cross network of Immunohematology Reference Laboratories (IRL) is the largest IRL system in the United States, with over 40 facilities. Specialists in our IRLs are sought-after participants in AABB inspections, industry standard committees, state boards and organizations. Many of our laboratory professionals speak at both domestic and international events, conduct continuing education opportunities including live learning events and clinical rotations for residents and fellows. Our National Reference Laboratory for Blood Group Serology (NRLBGS), National Neutrophil Laboratory, and National Reference Laboratory for Specialized Testing provide specialty testing to the entire nation.

Our notable size and technical experience allow us to serve a range of patients coping with diseases such as cancer, sickle cell disease and other hematologic diagnoses resulting in anemia. We regularly support hospital-based sickle cell disease management programs, as part of efforts to enhance treatment plans and overall patient care.

Red Cell Antibody Investigations

**Indication**

- As ordered by the hospital blood bank, pathologist or patient's physician.

**Description**

- Identification of red blood cell (RBC) antibodies to high prevalence, low prevalence, single and/or multiple antigens
- Evaluation of RBC autoantibodies
- Investigation of Direct Antiglobulin Test (DAT)-negative autoimmune hemolytic anemia
- Drug-Induced Immune Hemolytic Anemia Investigations
- RBC phenotyping of patients (also see Molecular Testing section)
- ABO discrepancy investigations
- Transfusion reaction investigations
- Investigations for Hemolytic Disease of the Fetus and Newborn (HDFN)
- Test of record crossmatching services (availability varies by location)

**Test Methods**
- Tube, gel and solid phase RBC adherence methods (may vary by location)
- Enhancements, serum neutralization and inhibition media
- Autologous, allogeneic and miscellaneous adsorptions
- Chemical treatment of RBCs and plasma
- Reticulocyte separations
- Elution techniques
- Titrations

**Antigen-Negative Blood Products**

**Indication**
- For patients with special red blood cell antigen negative requirements.

**Description**
Our IRLs maintain an inventory of known antigen types to assist hospitals with antigen-negative blood needs. IRLs work through the American Rare Donor Program (ARDP) to locate and obtain rare units not available in inventory. Services include:
- Single and multiple antigen-negative RBC units
- RBC units negative for high and low prevalence antigens
- Hemoglobin S negative RBC units
- Access to the ADRP for rare RBC components including RH allele matching for variant Rh antigens

**Antigen Matched RBC Units in the Management of Patients with Sickle Cell Disease**

**Indication**
- For patients undergoing RBC transfusion therapy for management of sickle cell disease.

**Description**
Due to chronic transfusions, alloimmunization to RBC antigens is a significant risk for many patients with sickle cell disease. Studies have shown that the transfusion of antigen-selected units is the standard of care for chronically transfused patients with sickle cell disease. This may facilitate the long-term management of these patients. IRLs provide units that are phenotypically matched for selected RBC antigens of the patient.
IgA Deficiency and Anti-IgA Testing

Indications
- Identification of IgA-deficient patients
- Investigation of transfusion-associated anaphylaxis

Description
IgA testing may be performed on serum or plasma samples from blood donors or patients who have not been transfused in the past four months to determine the absence of IgA and/or the presence of anti-IgA (for determination of the need for IgA-reduced cellular products or IgA-deficient plasma and derivatives for patients).

Test Method
- A sensitive Enzyme-Linked Immunosorbent Assay (ELISA), validated to measure IgA levels as low as 0.05mg/dL, is used to determine IgA deficiency.

Drug-induced Immune Hemolytic Anemia Evaluations

Indication
- Patients with hemolytic anemia with a temporal relationship to drug therapy. These patients usually have a positive direct antiglobulin test and usually no reactivity in an eluate prepared from their RBCs.

Description
In vitro drug-induced antibodies that are reactive in in vitro tests are in four general categories:

- Some drugs (e.g., penicillin and cephalosporins) bind firmly to RBCs. Normal RBCs can be coated with the drug, in vitro, and the patient’s serum and/or eluate from the patient’s RBCs is tested against the drug-coated RBCs to detect the presence of the drug-induced antibody.
- Many drugs will not covalently bond to RBCs, thus drug-coated RBCs cannot be prepared. Antibodies to such drugs are detected by incubating the patient’s serum with the drug and RBCs and looking for hemolysis, agglutination and/or positive antiglobulin tests.
- Some drugs can bind protein non-specifically, and some normal sera will be reactive when drug studies are performed. This may require manipulation of tests including dilution studies.
- Drug-independent antibodies will react with RBCs in vitro without any drug being present (i.e., they appear as autoantibodies).

Test Methods
- Patient’s serum/eluate tested against drug-treated RBCs
- Patient’s serum tested against RBCs in the presence of a drug
Monocyte Monolayer Assay

Indications
• Determination of suitability of incompatible blood transfusion using an *in vitro* (noninvasive) procedure to predict the *in vivo* extravascular hemolysis process. This testing is useful for IgG antibodies to a high incidence antigen or antibodies for which a specificity could not be determined, or for those with variable reports of clinical relevance.

Description
The Monocyte Monolayer Assay (MMA) is an *in vitro* procedure used to assist in predicting if incompatible blood can be transfused safely to a patient. The mononuclear cells are harvested from the whole blood of random healthy donors. The incompatible RBCs are sensitized with a fresh serum sample of the patient and incubated with the monocyte monolayer (obtained from layering the mononuclear cells onto a glass slide). RBCs are selected for sensitization based on the patient’s RBC antibodies. A source of fresh complement is added to the test system for all antibodies except those in the RH system.

The “normal” range is determined by the testing laboratory using *in vivo* correlation studies. Values below the normal range indicate that the antibody is clinically insignificant and is unlikely to cause overt transfusion reaction due to transfused antigen-positive RBCs. Values above the normal range indicate that the antibody may cause the accelerated destruction of antigen-positive RBCs and may result in a hemolytic transfusion reaction.

Test Method
• Monocyte Monolayer Assay

American Rare Donor Program

The American Red Cross is a founding member of the American Rare Donor Program (ARDP). Established over 20 years ago, ARDP exists to ensure that matching blood can be found for patients with rare blood needs. A person’s blood type is considered rare if it is found in less than one in 1,000 people. The rarer a person’s blood type, the more challenging the circumstances if that person suddenly needs matched blood for a transfusion.

By possessing the largest product inventory, the Red Cross is a major source for rare blood products. We provide 24 hours a day, 7 days a week support to the ARDP to ensure that all requests received are addressed as quickly as possible.