APPENDIX A.

Glossary

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5-azacytidine	An analog of the pyrimidine nucleoside cytidine. It is used primarily in the treatment of acute myeloid leukemia and myelodysplastic syndrome. It was also found to raise fetal hemoglobin levels but is not approved for use in the care of individuals with sickle cell disease.
Acute chest syndrome (ACS)	An acute illness characterized by fever and/or respiratory signs and symptoms, accompanied by a new pulmonary infiltrate involving at least one complete lung segment consistent with the presence of alveolar consolidation on a chest x ray.
Acute hepatic sequestration (AHS)	Liver enlargement below the right costal margin of greater than or equal to 3 cm for children and greater than or equal to 5 cm for adults from previous physical exam without other explanation and a 2 g/dL or greater drop in hemoglobin level over a few hours to days.
Acute intrahepatic cholestasis (AIC)	Rapidly developing interruption in the excretion of bile caused by obstruction within the liver associated with severe abnormalities of liver function tests and coagulation parameters.
α-gene deletion	Lack of one or more of the four alpha globin genes on chromosome 16.
Alloimmunization	An immunological response by the recipient against "foreign" non-self-antigens that may follow an erythrocyte transfusion and result in destruction of transfused erythrocytes.
Anterior chamber of eye	The space between the cornea and the iris containing aqueous fluid.
Autoimmunization	In transfusion medicine, the term refers to the development of an immune response to an individual's own erythrocytes, which may result in the destruction of erythrocytes.
Avascular necrosis	Bone death due to compromised blood supply of the bone.
Azotemia	An elevation of blood urea nitrogen (BUN) and serum creatinine above normal levels.
CAR β-haplotype	A variant of the beta chain of the sickle hemoglobin that is prevalent in the Central African Republic (CAR). Also known as Bantu (Ban) haplotype.

Case fatality rate	Percentage of persons diagnosed as having a specified disease who die as a result of that illness within a given time period.
Cellular rheology	In the case of erythrocytes, this term refers to the flow dynamics of red blood cells and their ability to negotiate microvasculature due to their elastic and plastic properties.
Central retinal artery occlusion (CRAO)	Blockage of the retinal artery.
Central sensitization	An event that follows repetitive painful stimuli and sensitizes the central nervous system so that it perceives innocuous stimuli as painful.
Cholangitis	A severe infection of the bile ducts.
Choledocholithiasis	The presence of gallstones in the common bile duct.
Cholestatic jaundice	Jaundice of the skin and/or sclera due to dysfunction of the hepatobiliary system.
Chronic kidney disease (CKD)	Either having a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for greater than or equal to 3 months with or without kidney damage or having evidence of kidney damage for greater than or equal to 3 months, with or without decreased GFR, manifested by either pathologic abnormalities or markers of kidney damage (i.e., proteinuria) independent of cause.
Chronic sickle cell pain	Pain that does not resolve and lasts for more than 3 months.
Dactylitis	A vaso-occlusive crisis involving one or often multiple small bones, and characterized by swelling and pain in the hands and/or feet, occurring in infants or young children.
Delayed hemolytic transfusion reaction (DHTR)	Hemolysis of donor erythrocytes 1–4 weeks after a transfusion, due to the development of alloantibodies by the recipient toward the donor erythrocyte.
Disease-modifying therapies	Treatments or drugs that impact the course of a disease by slowing the progression of the disease and decreasing the number of relapses.
Erythrocytapheresis	Removal of recipient erythrocytes prior to and/or during donor erythrocyte infusion. This requires the use of an apheresis device.
Exchange transfusion	Removal of recipient blood prior to and/or during donor erythrocyte infusion. This can be accomplished by erythrocytapheresis or by a manual method.
Fix complement	In transfusion medicine, this term refers to antigen-antibody complexes binding complement, leading to complement-mediated lysis of erythrocytes.

Fluorescein angiography	An eye test that uses a fluorescein dye and camera to examine the circulation in the retina and choroid.
FEV_1	Forced expiratory volume in 1 second. The amount of air which can be forcibly exhaled from the lungs in the first second of an exhalation. Usually reported as both liters and percent predicted comparing to people of the same age, gender, and height.
FVC	Forced vital capacity. The amount of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. Usually reported as both liters and percent predicted comparing people to similar age, gender, and height.
FEV_1/FVC Percent (%)	The ratio of FEV_1 to FVC, which tells the clinician what percentage of the total amount of air is exhaled from the lungs during the first second of forced exhalation. This is considered a clinical measure of obstructive lung disease.
Glomerular filtration rate (GFR)	The total of filtration rates of all functional kidney nephrons. The GFR is estimated by measuring markers such as creatinine and Cystatin C.
Hb	Hemoglobin.
HbA	Hemoglobin A, normal hemoglobin.
HbAS	Hemoglobin A plus sickle hemoglobin; the carrier state for sickle cell anemia, also known as sickle cell trait.
HbF	Fetal hemoglobin.
HbS	Sickle hemoglobin.
HBSα-Thal	Hemoglobin SS + α thalassemia.
HbSC	Sickle cell hemoglobin C disease.
HbSS	Homozygous sickle cell disease.
Hemoglobinopathy	A disorder characterized by an abnormality of the structure or function of hemoglobin.
HLA	Human Leukocyte Antigen system is the name of the major histocompatibility complex (MHC) in humans.
Hydroxyurea	A ribonucleotide reductase inhibitor, initially used to treat patients who had myeloproliferative disorders; also known as hydroxycarbamide.
Hyperhemolysis posttransfusion	A drop in hematocrit (hemoglobin concentration) below pretransfusion levels after transfusion. Often associated with reticulocytopenia and identification of alloantibodies.

Hypersplenism	Enlargement of the spleen associated with reduction in multiple blood cell types.
Hyperviscosity	An increase in the resistance of blood to flow through vessels. This can occur due to an increase hemoglobin concentration of circulating blood, which could trigger vaso-occlusion.
Hyphema	Blood in the anterior chamber of the eye.
Hyposthenuria	The inability to concentrate urine.
Indirect Coombs test	Blood bank test used to identify alloantibodies in serum produced in response to exposure to foreign non-self red blood cell antigens; also known as indirect antiglobulin test (IAT).
Interconception period	An 18- to 24-month interval between the birth of one child and the conception of the next.
Iontophoresis	The introduction of an ionized substance (as a drug) through intact skin by the application of a direct electric current.
Leukocyte reduced	Donor erythrocytes that are filtered to reduce the number of white blood cells.
Macroalbuminuria	Urinary excretion of albumin typically greater than 300 milligrams per 24 hours.
Mean corpuscular volume (MCV)	The average volume of red blood cells measured in femtoliters (fL).
Microalbuminuria	Urinary excretion of albumin, typically between 30 and 300 milligrams per 24 hours.
Moyamoya syndrome	A rare progressive cerebrovascular disorder caused by blocked arteries at the base of the brain in the basal ganglia.
Neuropathic pain	Pain caused by a lesion or disease of the central or peripheral somatosensory system.
Neuroplasticity	The ability of the central nervous system to change and adapt to new experiences.
Orbital compression syndrome (OCS)	Marked swelling around the eye associated with pain and visual disturbances resulting from avascular necrosis of the orbital bone.
Pain management protocol	A detailed written plan that provides guidance for dosing of analgesic agents to achieve pain management. Protocols can be written for an individual patient by the clinician who provides care and best understands analgesic needs during a vaso-occlusive crisis (VOC), or they can be

	developed as a more generic protocol, specific to patients with SCD, often with higher analgesic doses and more frequent dosing intervals. Protocols should be based upon the individual's pain score and analgesic history.
Partial exchange transfusion	Removal of a volume of recipient blood less than the total blood volume and replacement with donor erythrocytes.
Patient-controlled analgesia (PCA)	A drug-delivery system that uses an intravenous pump to dispense a preset dose of a narcotic analgesic when the patient pushes a button. The PCA dose allows the patient to administer a dose up to every 10 minutes if needed. Additional basal or continuous background infusions may or may not be required based upon the individual, analgesic history, and current needs. Orders are written to define the PCA dose administered and PCA time interval every time the patient presses the PCA button. A lock out, or maximum dose per hour, is also written as a part of the PCA orders.
PEFR	Peak expiratory flow rate. A measurement of how fast a person can exhale.
Posterior chamber of eye	The space behind the iris and in front of the lens filled with aqueous humor.
Preimplantation genetic diagnosis (PGD)	Testing performed on an embryo before it is transferred to the uterus to determine if it also carries a genetic abnormality when one or both genetic parents have a known genetic abnormality.
Priapism	A sustained, unwanted, painful penile erection lasting 4 or more hours.
Primary care provider	Internist, family physician, pediatrician, nurse practitioner, or physician assistant with a clinical focus on the provision of general health care for the patient.
Proliferative sickle retinopathy (PSR)	Growth of new vessels that emerge from the retinal vasculature at the interface of perfused and nonperfused retina in response to vascular growth factors produced by retinal ischemia. Also known as sea fan.
Proteinuria	Any urinary protein excretion greater than normal (less than 300 mg/day).
Pulmonary arterial hypertension (PAH)	An elevation of pulmonary arterial systolic pressure (PASP) (greater than 25 mmHg at rest or greater than 30 mmHg with exercise) determined by right heart catheterization.
Sickle cell anemia	Genotypes HbSS and HbSβ^0-thalassemia, which are associated with the most severe clinical manifestations, are commonly referred to as sickle cell anemia.

Sickle cell disease (SCD)	Sickle cell disease (SCD) is caused by inherited mutations involving the beta globin gene that result in the formation of an abnormal hemoglobin (hemoglobin S). Red blood cells, which contain a predominance of hemoglobin S, undergo shape change when low oxygen concentrations cause polymerization of the sickle hemoglobin. The damaged red blood cells become rigid and inflexible, occluding blood vessels and inducing tissue ischemia, pain, and organ damage. This process is accompanied by an inflammatory response and shortened red blood cell survival. These alterations may result in a wide variety of clinical manifestations. SCD genotypes (exhibit 1) include homozygosity of the sickle hemoglobin gene (HbSS) and the compound heterozygous conditions hemoglobin $S\beta^0$-thalassemia ($HbS\beta^0$), hemoglobin $S\beta^+$-thalassemia ($HbS\beta^+$), hemoglobin SC disease (HbSC), and other, much less prevalent combinations. HbSS, the most prevalent genotype, and $HbS\beta^0$ are commonly referred to as sickle cell anemia (SCA) and are associated with the most severe clinical manifestations.
Sickle vasculopathy	Multiple biological processes contribute to the pathogenesis of vasculopathy, including red cell sickling, inflammation and adhesion biology, coagulation activation, stasis, deficient bioavailability and excessive consumption of nitric oxide, excessive oxidation, and reperfusion injury physiology. This leads to abnormal vascular tone and activated, adhesive endothelium.
Simple transfusion	The infusion of donor erythrocytes without removal of recipient blood.
Stuttering priapism	Multiple self-limited episodes of priapism, each lasting less than 4 hours.
Transcranial Doppler ultrasonography (TCD)	A noninvasive method of analyzing blood flow velocity in the brain.
Tricuspid valve regurgitant jet velocity (TRV or TRJ)	Transthoracic echocardiographic determination of pulmonary hypertension. Elevated pulmonary artery pressure results require confirmation by right heart catheterization.
Urobilinogenuria	The presence of urobilinogen (a metabolite of bilirubin) in the urine.
Vaso-occlusive crisis (VOC)	Pain resulting from tissue ischemia as a result of blockage of blood vessels, occurring in a variety of vascular beds, but most commonly in the bone or bone marrow and requiring analgesic medication. Also known as sickle crisis, acute pain crisis, or vaso-occlusive episodes.

Vital capacity	The volume of air that can be expelled from the lungs from a position of full inspiration, with no limit to duration of inspiration; equal to inspiratory capacity plus expiratory reserve volume.
Vitreous chamber of eye	The vitreous chamber occupies the posterior 4/5ths of the eye. It consists of the space between the lens and the retina, and is filled with a transparent gel called the vitreous humor.
Vitreoretinal traction forces	Forces in the vitreous chamber of the eye due to trauma or the proliferation of the new fibrosed vessels that exert negative pressure on the retina, which, if severe, may cause retinal detachment.