

CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,)	CRF Module / Guideline
<b>RBC, Hemolysis and Erythropoiesis</b>						
Complete blood count with differentials	Quantification of major cellular blood components		Nivaggioni, V, Bouriche, L, Coito, S, et al. Use of Sysmex XN-10 red blood cell parameters for screening of hereditary red blood cell diseases and iron deficiency anaemia. Int J Lab Hematol. 2020; 00: 1– 8. <a href="https://doi.org/10.1111/ijlh.13278">https://doi.org/10.1111/ijlh.13278</a> Brown, W., Keeney, M. and Hedley, B.D. (2014), Initial performance evaluation of the UniCel® DxH slide maker/stainer Coulter® cellular analysis system. Int. Jnl. Lab. Hem., 36: 172-183. doi:10.1111/ijlh.12150 ERMENS, A.A.M., HOFFMANN, J.J.M.L., KROCKENBERGER, M. and Van WIJK, E.M. (2012), New erythrocyte and reticulocyte parameters on CELL-DYN Sapphire: analytical and preanalytical aspects. International Journal of Laboratory Hematology, 34: 274-282. doi:10.1111/j.1751-553X.2011.01391.x		Core	
Hb	quantification fo protein in RBC		Phenx		Core	
Reticulocyte Absolute Count	Number of new red blood cells in production		Mauro Buttarello, MD, Pietro Bulian, MD, Giorgio Farina, MD, Valeria Temporin, MD, Lucia Toffolo, MD, Ernesto Trabuio, MD, Paolo Rizzotti, MD, Flow Cytometric Reticulocyte Counting: Parallel Evaluation of Five Fully Automated Analyzers: An NCCLS-ICSH Approach, American Journal of Clinical Pathology, Volume 115, Issue 1, January 2001, Pages 100–111, <a href="https://doi.org/10.1309/M26B-1YNQ-VNU8-M1CE">https://doi.org/10.1309/M26B-1YNQ-VNU8-M1CE</a>		Core	Not unusual to request multiple reticulocyte counts post-therapy Important to be recording reticulocyte count in low resource countries
Reticulocyte %	% of erythrocytes that are reticulocytes		Phenx		Core	

CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,)	CRF Module / Guideline
Nucleated RBC	Number of nucleated RBC in peripheral blood		David H. Hwang, MD, David M. Dorfman, MD, PhD, Dick G. Hwang, MD, PhD, Patricia Senna, MT (ASCP), Olga Pozdnyakova, MD, PhD, Automated Nucleated RBC Measurement Using the Sysmex XE-5000 Hematology Analyzer: Frequency and Clinical Significance of the Nucleated RBCs, American Journal of Clinical Pathology, Volume 145, Issue 3, March 2016, Pages 379–384, <a href="https://doi.org/10.1093/ajcp/aqv084">https://doi.org/10.1093/ajcp/aqv084</a>		supplemental	Manual assessment
Hemoglobin characterization	Proportion of globin chains in a whole blood sample	Report result	Phenx		Core	<input type="checkbox"/> High performance liquid chromatography (HPLC) - preferred <input type="checkbox"/> Isoelectric focusing (IEF) - preferred <input type="checkbox"/> Capillary zone electrophoresis (CZE)
Determination of the proportion of RBCs expressing non-βS globin chains	Proportion of individual RBCs expressing fetal hemoglobin or engineered globin chains	Report result	<a href="#">Hebert, N, Rakotoson, MG, Bodivit, G, et al. Individual red blood cell fetal hemoglobin quantification allows to determine protective thresholds in sickle cell disease. Am J Hematol. 2020; 1– 11.</a>  doi: 10.1002/ajh.2593		Core	<input type="checkbox"/> Flow cytometry <input type="checkbox"/> Single Cell Western
LDH	Crude marker of cell turnover		Phenx		Core	
Total bilirubin			Phenx		Core	
Direct bilirubin			Phenx		Core	

CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,	CRF Module / Guideline
Soluble transferrin receptor			Alan E Mast, Morey A Blinder, Ann M Gronowski, Cara Chumley, Mitchell G Scott, Clinical utility of the soluble transferrin receptor and comparison with serum ferritin in several populations, Clinical Chemistry, Volume 44, Issue 1, 1 January 1998, Pages 45–51, <a href="https://doi.org/10.1093/clinchem/44.1.45">https://doi.org/10.1093/clinchem/44.1.45</a> Ilenia Infusino, Federica Braga, Alberto Dolci, MD, Mauro Panteghini, MD, Soluble Transferrin Receptor (sTfR) and sTfR/log Ferritin Index for the Diagnosis of Iron-Deficiency Anemia A Meta-Analysis, American Journal of Clinical Pathology, Volume 138, Issue 5, November 2012, Pages 642–649, <a href="https://doi.org/10.1309/AJCP16NTXZLZFAIB">https://doi.org/10.1309/AJCP16NTXZLZFAIB</a>		Core	
Erythropoietin levels					Supplemental	
Haptoglobin (detectable)			Phenx		Supplemental	Test is done in CLIA certified lab
D-dimers			Int J Hematol. 2013 Aug;98(2):158-63. doi: 10.1007/s12185-013-1392-y.; J Lab Clin Med . 1999 Oct;134(4):352-62.		Supplemental-Highly Recommended	
Cell free hemoglobin					Exploratory	Unreliable-suggest as a "to do item"
RBC microparticles	Quantitative determination of RBC microparticles present in whole blood sample		<a href="https://dx.doi.org/10.2450%2F2014.0136-14">https://dx.doi.org/10.2450%2F2014.0136-14</a>		Exploratory	Unreliable-suggest as a "to do item"
RBC Deformability	RBC Deformability (expressed as elongation index) - Current recommended instrument is the LORCCA with oxygenscan		<a href="https://dx.doi.org/10.1002%2Fajh.25443">https://dx.doi.org/10.1002%2Fajh.25443</a> . AND <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4469365/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4469365/</a>		Exploratory	

CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,)	CRF Module / Guideline
Dense cells	Proportion of dense RBCs present in whole blood		Bartolucci P, Brugnara C, Teixeira-Pinto A, et al. Erythrocyte density in sickle cell syndromes is associated with specific clinical manifestations and hemolysis. Blood. 2012;120(15):3136-3141.. Blood 2014; 123 (12): 1972. doi: <a href="https://doi.org/10.1182/blood-2014-01-552711">https://doi.org/10.1182/blood-2014-01-552711</a>		Exploratory	Unreliable suggest as a to-do item
RBC lifespan measurements	Measurement of RBC lifespan		Carbon monoxide or biotin labeling are preferred methods <a href="https://dx.doi.org/10.1159/000342232">https://dx.doi.org/10.1159/000342232</a>		Exploratory	
Hemopexin					Exploratory	
Hemoglobin electrophoresis or HPLC to determine proportion of HbS and anti-sickling Hb in	Proportion of globin chains in sorted reticulocytes	Report result	CLIA certification		Exploratory	<input type="checkbox"/> High performance liquid chromatography (HPLC) - preferred
Soluble P-selectin	Quantification of soluble P-selectin by ELISA or flow cytometry (CD62)		<a href="#">Ted Wun, Marilyn J. Telen, Lakshmanan Krishnamurti, Timothy L. McCavit, Laura M DeCastro, Henry Flanner, Frans A. Kuypers, Sandra K. Larkin, Seungshin Rhee, John L. Magnani, Helen M. Thackray; Pan-Selectin Antagonist Rivipansel (GMI-1070) Reduces Soluble E-Selectin Levels While Improving Clinical Outcomes in SCD Vaso-Occlusive Crisis. Blood 2014; 124 (21): 2704. doi: <a href="https://doi.org/10.1182/blood.V124.21.2704.2704">https://doi.org/10.1182/blood.V124.21.2704.2704</a></a>		Exploratory	<input type="checkbox"/> Flow cytometry <input type="checkbox"/> Elisa
ICAM-1	Cell surface glycoprotein expressed on endothelial and immune cells (CD54)				Exploratory	<input type="checkbox"/> Flow cytometry <input type="checkbox"/> Elisa
VCAM-1					Exploratory	<input type="checkbox"/> Flow cytometry
Various adhesion assays/particles					Exploratory	
<b>Inflammatory Markers</b>						
CRP			Phenx		Core	

CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,)	CRF Module / Guideline
Cytokine assays	serum level of IL2SR, IL2, interferon gamma, IL4, IL5, IL10, IL13, IL1B, IL6, IL8, TNF alpha, IL17	Report result	Phenx	pre-therapy/post-therapy prior to re-	Exploratory	
Immunologic Reconstitution: T cell development panel	composition of naïve, recent thymic emigrants (RTEs), activated, effector and memory T cells based on differential expression of CD3, CD4, CD8, CCR7, CD45RA, CD31, HLA-DR, and CD38 by flow cytometry	Report result	Balandya E, Reynolds T, Obaro S, Makani J. Alteration of lymphocyte phenotype and function in sickle cell anemia: Implications for vaccine responses. Am J Hematol. 2016 Sep;91(9):938-46. doi: 10.1002/ajh.24438. Epub 2016 Jul 14. PMID: 27237467; PMCID: PMC4987157.	pre-therapy/post-therapy prior to re-vaccination/post-therapy 4 weeks after vaccination	Supplemental	
Immunologic Reconstitution: B cell development panel	expression of CD19, CD20, CD27, CD21, CD10, CD38, CD24, IgM, and IgD to characterize the different B cell compartments	Report result	Balandya E, et al 2016	pre-therapy/post-therapy prior to re-vaccination/post-	Supplemental	

CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,	CRF Module / Guideline
Immunologic Reconstitution: Lymphocyte Mitogen, Antigen Screen	Measurement of human lymphocytes' proliferative responses to various stimuli is a fundamental technique used to assess their biological status and functions. Mitogens, such as plant lectins phytohemagglutinin (PHA), concanavalin A (Con A) and pokeweed mitogen (PWM), are able to nonspecifically stimulate lymphocyte proliferation and used to evaluate patient immune responsiveness. Lymphocyte proliferation response to antigens, such as Candida, tetanus toxoid and tuberculin purified protein derivative (PPD), are evaluated as a function of memory in cell-mediated immunity.	Report result (scintillation counter)	Balandya E, et al 2016	pre-therapy/post-therapy prior to re-vaccination/post-therapy 4 weeks after vaccination	core	
Immunologic Reconstitution:	serum IgG, IgA, IgM level	Report result	Balandya E, et al 2016	pre-therapy/post-	core	
Immunologic Reconstitution: Tetanus Titers	specific IgG to tetanus toxoid vaccine	Report result	Balandya E, et al 2016	pre-therapy/post-therapy prior to re-vaccination/post-	core	

CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,	CRF Module / Guideline
Immunologic Reconstitution: S. Typhi Titers	specific IgG to typhoid Virulence Antigen Polysaccharide accine	Report result	Bausch-Jurken MT, Verbsky JW, Gonzaga KA, Elms NP, Hintermeyer MK, Gauld SB, Routes JM. The Use of Salmonella Typhim Vaccine to Diagnose Antibody Deficiency. J Clin Immunol. 2017 Jul;37(5):427-433. doi: 10.1007/s10875-017-0406-6. Epub 2017 Jun 7. PMID: 28589420.	pre-therapy/post-therapy prior to re-vaccination/post-therapy 4	core	
Immunologic Reconstitution: Pneumococcal Titers	specific IgGs to nonconjugated 23-valent and conjugated 13-valent vaccine	Report result	Balandya E, et al 2016	pre-therapy/post-therapy prior to re-vaccination/pos	core	
<b>Other exploratory assays</b>						
Inflammation-ischemia reperfusion assays					Exploratory	
Vasculopathy/endothelial activation assays					Exploratory	
Molecular assays (proteomics/epigenetics/metabolomics)					Exploratory	
<b>Gene Therapy Specific Assays</b>						
VCN, INDELS or percentage of correction in peripheral	Bulk VCN/Editing/Correction in a whole blood sample	Report result			Core	
Proportion of transduced, edited or corrected cells in peripheral blood	Single cell assessment of transduction/editing/correction	Report results			Core	
<b>Drug Product Release Assays</b>						
Purity	Proportion of CD34+ cells (of CD45+)		<a href="https://www.fda.gov/media/113760/download">https://www.fda.gov/media/113760/download</a>		Core	
Identity	Confirm/quantify production of globin chain of interest		<a href="https://www.fda.gov/media/113760/download">https://www.fda.gov/media/113760/download</a>		Core	
VCN, INDELS or Correction			<a href="https://www.fda.gov/media/113760/download">https://www.fda.gov/media/113760/download</a>		Core	
off-target editing			<a href="https://www.fda.gov/media/113760/download">https://www.fda.gov/media/113760/download</a>		Core	
CFC Assay			<a href="https://www.fda.gov/media/113760/download">https://www.fda.gov/media/113760/download</a>		Core	

CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,)	CRF Module / Guideline
Potency Assay	Additional drug product potency assay to measure the "intended biological effect" as to be determined by sponsor based on MOA of product		<a href="https://www.fda.gov/media/79856/download">https://www.fda.gov/media/79856/download</a>		Core	
<b>Genetic Diagnostic Testing for Sickle Cell</b>						
Laboratory Procedure Hemoglobin Analysis Method Type	The method use for hemoglobin analysis.	<input type="checkbox"/> High performance liquid chromatography (HPLC) - preferred <input type="checkbox"/> Isoelectric focusing (IEF) - preferred <input type="checkbox"/> Capillary zone electrophoresis (CZE) <input type="checkbox"/> Gel electrophoresis <input type="checkbox"/> Point of Care (consideration for low resource geographies) <input type="checkbox"/> Other	<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Hemoglobin Analysis Other Method Specify			<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Hemoglobin S Result Percentage Value			<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Hemoglobin C Result Percentage Value			<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	



CDE Name	Definition / Description	Permissible Value	References	Population	Classification (e.g.,)	CRF Module / Guideline
Laboratory Procedure Hemoglobin F Result Percentage Value			<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Hemoglobin A Result Percentage Value			<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Hemoglobin A2 Result Percentage Value			<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Hemoglobin Genetic Modified A Variant Result			<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Hemoglobin Other Result Percentage Value			<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Hemoglobin Other Result Specify	The free-text field to specify the other result in the hemoglobin analysis result.		<a href="https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf">https://www.aphl.org/aboutAPHL/publications/Documents/NBS_HemoglobinopathyTesting_122015.pdf</a>		Core	
Laboratory Procedure Alpha and Beta					Core	