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| **About the Measure** | |
| **Domain:** | Sickle Cell Disease Core: Tier 1 |
| **Measure:** | Hemoglobin Characterization |
| **Definition:** | A bioassay for hemoglobin classification. |
| **Purpose:** | This protocol can be used to identify and characterize the different variants in structure and synthesis of hemoglobin that cause sickle cell disease. |
| **Essential PhenX Measures:** | Biological Sex Assigned at Birth  Complete Blood Count (CBC)  Current Age  Gender Identity  History of Transfusion  Medication Inventory |
| **Related PhenX Measures:** | Aspartate Aminotransferase Level  Bilirubin Level  Haptoglobin Level  Lactate Dehydrogenase Level  Reticulocyte Count |
| **Measure Release Date:** | July 30, 2015 |

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| **About the Protocol** | |
| **Protocol Release Date:** | July 30, 2015 |
| **PhenX Protocol Name:** | Hemoglobin Characterization |
| **Keywords:** | hemoglobin characterization, sickle cell disease, SCD, SC disease, anemia, thalassemia, hemoglobin, hemoglobinopathy, high-performance liquid chromatography, HPLC, isoelectric focusing, IEF, immunoassay |
| **Protocol Name from Source:** | The Laboratory Diagnosis of Haemoglobinopathies, 1998 |
| **Description:** | This protocol provides basic instructions for drawing and storing blood and performing the bioassay for hemoglobin characterization. Because there are many assays that may be required to characterize hemoglobin abnormalities, the protocol also provides basic guidelines to increase comparability among different studies. |
| **Specific Instructions:** | The Sickle Cell Disease Research and Scientific Panel (SRSP) recommends that investigators also capture Complete Blood Count and Reticulocyte Count.  The SRSP recommends that results from Hemoglobin Characterization be interpreted in the context of age appropriate normal values and blood transfusions within the last 120 days.  The results of the Hemoglobin Characterization can be interpreted using the hemoglobinopathy case definition worksheets and classification tables from the Newborn Screening Technical Assistance and Evaluation Program (NewSTEPS, see [Sickle Cell Disease Case Definitions](http://www.phenxtoolkit.org/toolkit_content/supplemental_info/scd_core_tier_1/measures/Sickle_Cell_Disease_Case_Definitions.doc)) funded by the Health Resources and Services Administration (HRSA). Investigators complete the case definition worksheets using available clinical data including: family history of hemoglobin variants, hemoglobin newborn screening results, laboratory record of complete blood count (CBC) with mean corpuscular volume (MCV), hemoglobin electrophoresis, isoelectric focusing, high performance liquid chromatography, and DNA genotype. Investigators then use the associated classification tables to interpret the results and make a diagnosis. The classification tables indicate the level of certainty (e.g., definite, probable, possible, or unlikely) of the diagnosis based on the type of clinical data available. |
| **Protocol:** | **Hemoglobin Characterization**  **Blood Draw**  Blood should be drawn into an appropriate EDTA tube.  **Laboratory Assay for Hemoglobin Characterization**  The Sickle Cell Disease Scientific and Research Panel (SRSP) notes that there are numerous different assays and instruments (e.g., hemoglobin electrophoresis, isoelectric focusing, high performance liquid chromatography, DNA sequencing analysis) that are appropriate to characterize hemoglobin variants. Once an assay is chosen for a particular study, the SRSP recommends that no changes in the protocol be made over the course of the study. To aid comparability, the SRSP recommends that the investigator record the make and manufacturer of equipment used and the repeatability and coefficients of variation for the assay.  The SRSP notes that investigators should record the assay results for the following hemoglobins (the exact list of hemoglobins that can be distinguished will depend on the assay being used). The hemoglobins are listed in order of the amount present with the most prevalent coming first.   * A * F * S * C * E/A2 * D-Punjab * G-Philadelphia * O-Arab |
| **Selection Rationale:** | The Laboratory Diagnosis of Haemoglobinopathies (1998) was compared to other protocols and selected by the Sickle Cell Disease Research and Scientific Panel (SRSP) because it includes advantages and disadvantages of the various techniques as well as the ability of the assays to separate the various hemoglobin variants. |
| **Source:** | The Laboratory Diagnosis of Haemoglobinopathies. (1998). British Journal of Haematology, 101(4), 783-792. doi: 10.1046/j.1365-2141.1998.00809.x |
| **Availability:** | Available |
| **Life Stage:** | Infant, Toddler, Child, Adolescent, Adult, Senior, Pregnancy |
| **Language:** | English |
| **Participant:** | All ages |
| **Personnel and Training Required:** | Phlebotomist |
| **Equipment Needs:** | CLIA certified laboratory with the capability to perform the hemoglobin assay. |
| **General References:** | Kutlar, F. (2007). Diagnostic approach to hemoglobinopathies. Hemoglobin, 31(2), 243-250.  Kutlar, A., & Huisman, T. (1996). Detection of hemoglobinopathies. In F. Hommes (Ed.), Techniques in Diagnostic Human Biochemical Genetics: A Laboratory Manual (pp. 519-560). New York, New York: J. Wiley & Sons. |
| **Mode of Administration:** | Bioassay |
| **Derived Variables:** | None |
| **Requirements:** | |  |  | | --- | --- | | **Requirements Category** | **Required (Yes/No):** | | Major equipment | No | | Specialized training | No | | Specialized requirements for biospecimen collection | No | | Average time of greater than 15 minutes in an unaffected individual | No | |
| **Annotations for Specific Conditions:** | None |
| **Process and Review:** |  |