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| **About the Measure** | |
| **Domain:** | Sickle Cell Disease Pregnancy |
| **Measure:** | Cell-free fetal DNA testing |
| **Definition:** | Cell-free fetal DNA testing is used to examine fetal DNA circulating in a pregnant person’s blood stream. |
| **Purpose:** | Cell-free fetal DNA testing is a relatively low-burden, low-risk way to test for chromosomal and genetic abnormalities (e.g., down syndrome, sickle cell disease) prior to birth. For sickle cell disease, cell-free fetal DNA testing is still considered a research investigation and not standard of clinical care. |
| **Essential PhenX Measures:** | NA |
| **Related PhenX Measures:** | NA |
| **Measure Release Date:** | NA |

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| **About the Protocol** | |
| **Protocol Release Date:** | TK Team to add |
| **PhenX Protocol Name:** | Cell-free Fetal DNA Testing for Sickle Cell Disease |
| **Keywords:** | NA |
| **Protocol Name from Source:** | A method for noninvasive prenatal diagnosis of monogenic autosomal recessive disorders. |
| **Description:** | This protocol summarizes the method described in Cutts et al, (2019). |
| **Specific Instructions:** | None |
| **Protocol:** | **Cell-free fetal DNA Testing**  The article by Cutts et al (2019) describes a method for diagnosing sickle cell disease in fetuses using cell-free fetal DNA testing combined with next generation sequencing. The authors describe the overall method, including PCR primers, library preparation, and statistical analysis. |
| **Selection Rationale:** | The PhenX Sickle Cell Disease Pregnancy Working Group (WG) selected the approach outlined in Cutts et al (2019) as the gold-standard for diagnosing sickle cell disease from cell-free fetal DNA. The WG recommended it be included in Supplemental Information due to investigator burden. |
| **Source:** | Cutts, A., Vavoulis, D. V., Petrou, M., Smith, F., Clark, B., Henderson, S., & Schuh, A. (2019). A method for noninvasive prenatal diagnosis of monogenic autosomal recessive disorders. *Blood*, *134*(14), 1190–1193. <https://doi.org/10.1182/blood.2019002099>  Ghi, T., Sotiriadis, A., Calda, P., Da Silva Costa, F., Raine-Fenning, N., Alfirevic, Z., McGillivray, G., & International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) (2016). ISUOG Practice Guidelines: invasive procedures for prenatal diagnosis. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*, *48*(2), 256–268. <https://doi.org/10.1002/uog.15945> |
| **Availability:** | Available |
| **Life Stage:** | Adolescent, adult |
| **Language:** | English |
| **Participant:** | Pregnant people with sickle cell disease |
| **Personnel and Training Required:** | Staff capable of extracting blood and performing cell-free fetal DNA testing (e.g., qPCR, library amplification, next generation sequencing, and statistical analysis). |
| **Equipment Needs:** | Laboratory and equipment capable of performing qPCR, library amplification, and next generation sequencing. |
| **General References:** | Hanson, B., Scotchman, E., Chitty, L. S., & Chandler, N. J. (2022). Non-invasive prenatal diagnosis (NIPD): how analysis of cell-free DNA in maternal plasma has changed prenatal diagnosis for monogenic disorders. *Clinical science*. *136*(22),1615–1629. <https://doi.org/10.1042/CS20210380> |
| **Mode of Administration:** | Medical record abstraction |
| **Derived Variables:** | None |
| **Requirements:** | |  |  | | --- | --- | | **Requirements Category** | **Required (Yes/No):** | | Major equipment | Y | | Specialized training | Y | | Specialized requirements for biospecimen collection | Y | | Average time of greater than 15 minutes in an unaffected individual | N | |
| **Annotations for Specific Conditions:** | None |
| **Process and Review:** | NA |